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ligand), and **OX40**, have also been implicated in the survival, generation, maintenance, and quality of **virus**-specific memory CD8+ T cells. The delivery of costimulatory mols. such as CD28, **4-1BB**, and **OX40** can help boost the generation and function of **virus**-specific memory CD8+ T cells. The use of costimulatory mols. as adjuvants, along with viral antigens in vaccines, may facilitate the generation of effective antigen-specific memory CD8+ T-cell responses. Understanding the costimulatory requirements of memory CD8+ T cells, therefore, may lead to improved vaccines that target anti-viral CD8+ T-cell memory.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
(1 CITINGS)

REFERENCE COUNT: 138 THERE ARE 138 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L17 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2009:1626269 CAPLUS

DOCUMENT NUMBER: 152:589804

TITLE: Expressions of activating and inhibitory receptors as
well as costimulatory molecules on peripheral blood
natural killer cells in patients with recurrent
genital herpes

AUTHOR(S): Qian, Qifeng; Zhen, Lin; Li, Qing

CORPORATE SOURCE: Center for STD Control and Research, Shenzhen
Institute of Dermatology, Shenzhen, Guangdong
Province, 518020, Peop. Rep. China

SOURCE: Zhonghua Pifuke Zazhi (2009), 42(5), 308-310
CODEN: CHFTAJ; ISSN: 0412-4030

PUBLISHER: Zhongguo Yixue Kexueyuan Pifubing Yanjiuso

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB The expressions of activating receptors (NKG2D and NKp46), inhibitory
receptors (NKG2A and KIR) as well as costimulatory mols. (**OX40**, **4-1BB**
and **ICOS**) on peripheral blood natural killer (NK) cells from patients with
recurrent genital herpes (RGH) were investigated. Four-color
immunofluorescence staining with flow cytometry was used to detect the
expression of NKG2D, NKG2A, KIR and NKp46 in 44 patients with RGH and 40
normal human controls, and to detect the expressions of **OX40**, **4-1BB**
and **ICOS** in 29 patients with RGH and 29 normal human controls. The
proportions of NKG2D-pos. and NKp46-pos. NK cells significantly decreased
in patients with RGH than those in the normal human controls
[(93.3±5.4)% vs. (96.9±2.5)%, (88.9±8.7)% vs.
(93.4±4.1)%, resp., both P<0.01]. Between the patients and the
controls, no significant difference was obsd. in the expression of NK cell
inhibitory receptors, NKG2A [(41.8±14.4)% vs. (46.0 ± 14.7)%,
P>0.05] or KIR [(68.3±19.1)% vs. (69.1±17.6)%, P>0.05]. A lower
expression of costimulatory mol. **OX40** was noted in NK cells from
patients with RGH compared with those in normal controls [(1.0±1.1)%
vs. (1.8±1.7)%, P<0.05]. Herpes simplex **virus** infection could
down-regulate the expression of NK cell activating receptors and
costimulatory mols., subsequently suppress the activation of NK cells, and
lead to the escape of **virus**-infected cells from the killing of NK cells.

L17 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2009:1616023 CAPLUS
 DOCUMENT NUMBER: 152:104837
 TITLE: Therapeutic agents comprising elastin-like peptides fused to therapeutic proteins for improved pharmacodynamics
 INVENTOR(S): Chilkoti, Ashutosh
 PATENT ASSIGNEE(S): Duke University, USA
 SOURCE: PCT Int. Appl., 214pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 2009158704</u>	A2	20091230	<u>WO 2009-US49059</u>	20090629
<u>WO 2009158704</u>	A3	20100318		
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
<u>CA 2726894</u>	A1	20091230	<u>CA 2009-2726894</u>	20090629
<u>US 20100022455</u>	A1	20100128	<u>US 2009-493912</u>	20090629
<u>PRIORITY APPLN. INFO.:</u>			<u>US 2008-76221P</u>	P 20080627
			<u>WO 2009-US49059</u>	W 20090629

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 152:104837

AB The present invention provides therapeutic agents and compns. comprising elastin-like peptides (ELPs) and therapeutic proteins. The therapeutic protein may be a glucagon-like peptide-1 (GLP-1) receptor agonist, insulin, or blood-coagulation factor VII/VIIa, including functional analogs. The present invention further provides encoding polynucleotides, as well as methods of making and using the therapeutic agents. The therapeutic agents have improvements in relation to their use as therapeutics, including, inter alia, one or more of half-life, clearance, and/or persistence in the body, soly., and bioavailability. Thus, human factor VII was fused by its C-terminus to ELP1-90, which comprises the VPGXG motif where X is a Val, Gly, or Ala in the ratio 5:3:2 in a 10-unit repeat, repeated 8x with a final C-terminal 10-unit repeat where X is a Val, Gly, Ala, and Cys in the ratio 4:3:2:1. When administered to rats by i.v., factor VII-ELP1-90 demonstrated a half-life of about 690 min, whereas factor VII demonstrated a half-life of 45-50 min.

L17 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2009:1556173 CAPLUS
 DOCUMENT NUMBER: 153:141678
 TITLE: Timing and tuning of CD27-CD70 interactions: the

impact of signal strength in setting the balance between adaptive responses and immunopathology

AUTHOR(S): Nolte, Martijn A.; van Olfen, Ronald W.; van Gisbergen, Klaas P. J. M.; van Lier, Rene A. W.

CORPORATE SOURCE: Department of Experimental Immunology, Academic Medical Center, University of Amsterdam, Amsterdam, Neth.

SOURCE: Immunological Reviews (2009), 229(1), 216-231
 CODEN: IMRED2; ISSN: 1600-065X
 URL: <http://www3.interscience.wiley.com/cgi-bin/fulltext/122341683/PDFSTART>

PUBLISHER: John Wiley & Sons, Inc.

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

AB A review. After binding its natural ligand cluster of differentiation 70 (CD70), CD27, a tumor necrosis factor receptor (TNFR)-assocd. factor-binding member of the TNFR family, regulates cellular activity in subsets of T, B, and natural killer cells as well as hematopoietic progenitor cells. In normal immune responses, CD27 signaling appears to be limited predominantly by the restricted expression of CD70, which is only transiently expressed by cells of the immune system upon activation. Studies performed in CD27-deficient and CD70-transgenic mice have defined a non-redundant role of this receptor-ligand pair in shaping adaptive T-cell responses. Moreover, adjuvant properties of CD70 have been exploited for the design of anti-cancer vaccines. However, continuous CD27-CD70 interactions may cause immune dysregulation and immunopathol. in conditions of chronic immune activation such as during persistent **virus** infection and autoimmune disease. We conclude that optimal tuning of CD27-CD70 interaction is crucial for the regulation of the cellular immune response. We provide a detailed comparison of costimulation through CD27 with its closely related family members 4-1BB (GD137), CD30, herpes **virus** entry mediator, **OX40 (CD134)**, and glucocorticoid-induced TNFR family-related gene, and we argue that these receptors do not have a unique function per se but that rather the timing, context, and intensity of these costimulatory signals det. the functional consequence of their activity.

OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)

REFERENCE COUNT: 144 THERE ARE 144 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2009:839403 CAPLUS

DOCUMENT NUMBER: 151:334741

TITLE: Decreased 4-1BB expression on HIV-specific CD4+ T cells is associated with sustained viral replication and reduced IL-2 production

AUTHOR(S): Kassu, Afework; D'Souza, Michelle; O'Connor, Brian P.; Kelly-McKnight, Elizabeth; Akkina, Ramesh; Fontenot, Andrew P.; Palmer, Brent E.

CORPORATE SOURCE: Division of Allergy and Clinical Immunology, Department of Medicine, University of Colorado Denver, Aurora, CO, 80045, USA

SOURCE: Clinical Immunology (Amsterdam, Netherlands) (2009), 132(2), 234-245
 CODEN: CLIIFY; ISSN: 1521-6616

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal
 LANGUAGE: English

AB CD4+ T cell dysfunction in subjects with chronic HIV infection is in part due to an imbalance of costimulatory and coinhibitory receptors. The authors report that **virus**-specific CD4+ T cells expressing 4-1BB (CD137) or **OX40 (CD134)** produced more IL-2 than cells lacking these costimulatory receptors and that 4-1BB was expressed at a lower level on HIV- than CMV-specific IFN- γ and IL-2 producing CD4+ T cells. Suppression of viral replication with antiretroviral therapy was assocd. with increased 4-1BB expression on HIV- and CMV-specific IL-2 producing CD4+ T cells and the percentage of IL-2 producing HIV-specific CD4+ T cells that expressed 4-1BB was inversely correlated with HIV plasma viral load ($r = -0.75$). These findings indicate that the loss of 4-1BB on HIV-specific CD4+ T cells is assocd. with viral replication and that it may contribute to reduced IL-2 prodn. obsd. during chronic infection.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2007:1114762 CAPLUS

DOCUMENT NUMBER: 147:404820

TITLE: Modulation of immune system components for treatment of respiratory **virus** infections using a composition comprising a molecular blockade agent to a costimulatory mol.

INVENTOR(S): Hussell, Tracy; Larrick, James W.; Foltin, George L.

PATENT ASSIGNEE(S): Imperial Innovations Limited, UK

SOURCE: PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 2007111931</u>	A2	20071004	<u>WO 2007-US7098</u>	20070322
<u>WO 2007111931</u>	A3	20071129		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
<u>EP 2010207</u>	A2	20090107	<u>EP 2007-753704</u>	20070322
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS			
<u>JP 2009530391</u>	T	20090827	<u>JP 2009-501555</u>	20070322
<u>US 20100015143</u>	A1	20100121	<u>US 2009-225459</u>	20090424

PRIORITY APPLN. INFO.:

US 2006-785407P

P 20060322

WO 2007-US7098

W 20070322

AB A compn. comprising a mol. blockade agent to a costimulatory mol. which costimulatory mol. satisfies the following criteria: (1) absent in naive or resting T-lymphocytes; (2). inducible; (3). expressed; and (4). prominent at the height of an immunopathol. response, such as a disease/condition response. Preferably, the costimulatory mol. is **OX40** and the mol. blockade agent is an antibody or antibody fragment having antibody activity to **OX40**. In the examples the inventors use a PEGylated anti-**OX40** antibody (A9) to block the interaction between **OX40** on T cells and **OX40** ligand on antigen-presenting cells in mouse model of respiratory syncytial **virus** and influenza **virus** infection.

L17 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2007:1091580 CAPLUS
 DOCUMENT NUMBER: 148:353490
 TITLE: Inhibition of **OX40**-Ig on herpetic stromal keratitis in murine model
 AUTHOR(S): Xia, Likun; Chen, Xiaolong; Zhu, Yingming; Zhou, Jing
 CORPORATE SOURCE: Department of Ophthalmology, Affiliated Second Hospital, China Medical University, Shenyang, 110004, Peop. Rep. China
 SOURCE: Yanke Yanjiu (2006), 24(5), 479-483
 CODEN: YAYAFH; ISSN: 1003-0808
 PUBLISHER: Henan Institute of Ophthalmology
 DOCUMENT TYPE: Journal
 LANGUAGE: Chinese

AB Herpetic stromal keratitis (HSK) is an immunoinflammatory lesion in the cornea of the eye set off by the infection with HSV-1. The disease appears to be orchestrated by CD4+ T cells. In current study, it was investigated that the inhibition of **OX40**-Ig on the inhibition of HSK. Corneas of right eyes from 90 BALB/c mice were infected with 106 PFU of HSV-1 McKrae strain. Mice were injected i.p. with **OX40**-Ig or IgG Fc or PBS given on day 0, 2, 4 after the infection. CD4+ T cells from peripheral blood of mice were analyzed on FACS 440 analyzer. The clin. evaluations of infected eyes were taken under the slit-lamp microscope, and the histol. changes of corneas were obsd. under the optical microscope. **Virus** titers in corneas after HSV-1 infection were tested with VERO cells, and delayed type hypersensitivity was obsd. The effects of **OX40**-Ig on HSK were evaluated. As measured by flow cytometry, in the mice treated with **OX40**-Ig, 78.2% of CD4+ T cells were reduced. 83.3% Of the HSV-1-infected control mice developed severe stromal keratitis, but only 20.0% of mice treated by **OX40**-Ig developed HSK. Lesions in **OX40**-Ig treated mice showed markedly reduced severity by slit-lamp microscope, and histol. the corneal stroma had a decrease in inflammatory cell infiltration compared to the control group, and the delayed type hypersensitivity was reduced. The results provide an evidence that blockade of OX-40/OX-40L co-stimulation by **OX40**-Ig can inhibit the proliferation of CD4+ T cells and impair onset and severity of HSK.

L17 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2006:1114150 CAPLUS
 DOCUMENT NUMBER: 146:204173
 TITLE: Anti-**OX40** (**CD134**) Administration to Nonhuman Primates: immunostimulatory Effects and Toxicokinetic Study

AUTHOR(S) : Weinberg, Andrew D.; Thalhoffer, Colin; Morris, Nick; Walker, Joshua M.; Seiss, Donald; Wong, Scott; Axthelm, Michael K.; Picker, Louis J.; Urba, Walter J.
 CORPORATE SOURCE: Providence Portland Medical Center, Robert W. Franz Cancer Center, Earle A. Chiles Research Institute, Portland, OR, 5F40, USA
 SOURCE: Journal of Immunotherapy (2006), 29(6), 575-585
 CODEN: JOIMF8; ISSN: 1524-9557
 PUBLISHER: Lippincott Williams & Wilkins
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The immune-stimulatory properties of anti-**CD134 (OX40)** antibodies have been well documented in rodents, including their ability to enhance antitumor immunity. In this study, an anti-**OX40** antibody (Ab) known to costimulate monkey T cells in vitro, was infused into rhesus macaque monkeys during immunization with the simian immunodeficiency **virus** protein, gp130. The draining lymph nodes from immunized monkeys treated with anti-**OX40** were enlarged compared with immunized monkeys injected with mouse Ig. Anti-**OX40**-treated monkeys had increased gp130-specific Ab titers, and increased long-lived T-cell responses, compared with controls. There were no overt signs of toxicity in the anti-**OX40**-treated monkeys. The encouraging immune-stimulatory effects led to the good manufg. practice prodn. of an anti-**OX40** Ab for clin. trials in cancer patients. A detailed toxicol. study was performed with anti-**OX40** in nonhuman primates. Three groups of 8 monkeys received anti-**OX40** at 1 of 3 dose levels (0.4, 2.0, and 10 mg/kg) and a control group received saline. No clin. toxicity was obsd., but acute splenomegaly and enlarged gut-assocd. lymph nodes were obsd. in the anti-**OX40**-treated animals; splenomegaly and lymphadenopathy resolved by day 28. These studies demonstrate the immune-stimulatory properties and safety of anti-**OX40** in primates and provide a strong scientific rationale to pursue clin. trials in humans.

OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)
 REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2004:706197 CAPLUS
 DOCUMENT NUMBER: 141:348613
 TITLE: Factors that increase the effective concentration of CXCR4 dictate feline immunodeficiency **virus** tropism and kinetics of replication
 AUTHOR(S) : de Parseval, Aymeric; Ngo, Stacie; Sun, Peiqing; Elder, John H.
 CORPORATE SOURCE: Department of Molecular Biology, The Scripps Research Institute, La Jolla, CA, USA
 SOURCE: Journal of Virology (2004), 78(17), 9132-9143
 CODEN: JOVIAM; ISSN: 0022-538X
 PUBLISHER: American Society for Microbiology
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The surface glycoprotein (gp95) of the feline immunodeficiency **virus** (FIV) binds in a strain-specific manner to several cell surface mols., including CXCR4, heparan sulfate proteoglycans (HSPGs), DC-SIGN, and a 43-kDa cell surface receptor on T cells recently identified as **CD134** by M. Shimojima et al. CXCR4 is the entry receptor in all known cases, and the other mols. act as binding receptors to help facilitate infection. In

this report, the authors confirm and extend the findings regarding **CD134** as a primary receptor for FIV. In addn., the authors show that temp. critically influences the binding properties of FIV gp95 to CXCR4 and HSPGs. The data show that gp95 of the field strain FIV-PPR bound to CXCR4 at 22°, whereas binding was not detected at 4°. In contrast, binding of the lab. adapted FIV-34TF10 gp95 was obsd. at either 4° or 22°, albeit at increased levels at the higher temp. The level of CXCR4 increased after the temp. was switched from 4 to 22°, whereas the level of HSPGs decreased, resulting in higher binding of gp95 from both strains to CXCR4 and lower binding of gp95 of FIV-34TF10 to HSPGs (FIV-PPR gp95 does not bind to these mols.). The findings also show that HSPGs facilitate the CXCR4-mediated infectivity of CrFK and G355-5 cells by FIV-34TF10. These two nonlymphoid cell lines express very low levels of CXCR4 and are permissive to FIV-34TF10 but not to productive infection by FIV-PPR. However, overexpression of human CXCR4 in CrFK or G-355-5 cells resulted in extensive cell fusion and infection by FIV-PPR. Taken together, these findings indicate that factors that increase the effective concn. of CXCR4 enhance FIV infectivity and may involve (i) temp. or ligand-induced conformational changes in CXCR4 that enhance SU binding, (ii) coreceptor interactions with gp95 that either alter gp95 conformation to enhance CXCR4 binding and/or raise the localized concn. of receptor or ligand, or (iii) direct increase in CXCR4 concn. via overexpression.

OS.CITING REF COUNT: 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS RECORD (20 CITINGS)
 REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2004:676377 CAPLUS
 DOCUMENT NUMBER: 141:312868
 TITLE: **4**-1BB and **OX40** stimulation enhance CD8 and CD4 T-cell responses to a DNA prime, poxvirus boost vaccine
 AUTHOR(S): Munks, Michael W.; Mourich, Dan V.; Mittler, Robert S.; Weinberg, Andrew D.; Hill, Ann B.
 CORPORATE SOURCE: Department of Molecular Microbiology and Immunology, Oregon Health and Science University, Portland, OR, USA
 SOURCE: Immunology (2004), 112(4), 559-566
 CODEN: IMMUAM; ISSN: 0019-2805
 PUBLISHER: Blackwell Publishing Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB **4**-1BB (CD137) is a tumor necrosis factor receptor (TNFR) family member, expressed primarily on CD8 T cells after activation. Signaling through **4**-1BB has been reported to enhance CD8 T-cell expansion and to protect activated CD8 T cells from death, resulting in an enlarged memory population. Although stimulating **4**-1BB has been shown to significantly improve the immune response to weak immunogens such as tumors, little is known about its effect on the CD8 T-cell response to a powerful viral vector such as vaccinia. To test **4**-1BB's ability to improve the murine CD8 T cell response to a DNA prime, poxvirus boost vaccine, similar to those used for human immunodeficiency **virus** and simian immunodeficiency **virus** vaccines, we administered **4**-1BB agonist antibody at the time of the poxvirus boost. **4**-1BB stimulation increased the no. of functional memory CD8 T cells by two- to fourfold. However, we saw a similar enhancement at the peak of the response and in the memory phase, thus we

found no evidence in the context of **virus** infection that **4-1BB** stimulation could increase the percentage of CD8 T cells that survive the acute activation phase to become memory cells. **OX40 (CD134)** is an analogous TNFR family member expressed primarily on activated CD4 T cells. **OX40** stimulation increased the no. of antigen-specific CD4 T cells approx. threefold. Stimulating both **4-1BB** and **OX40** enhanced the CD8 T-cell response more than **4-1BB** alone. Thus stimulating these receptors can improve the response to a powerful **virus** vector, and may be useful in vaccine development.

OS.CITING REF COUNT: 21 THERE ARE 21 CAPLUS RECORDS THAT CITE THIS RECORD (21 CITINGS)
 REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 1998:684978 CAPLUS
 DOCUMENT NUMBER: 129:274700
 ORIGINAL REFERENCE NO.: 129:56017a,56020a
 TITLE: DNA encoding targeting protein fused to antigen or epitope in enhancement of immune response to DNA vaccines
 INVENTOR(S): Boyle, Jefferey Stephen; Brady, Jamie Louise; Lew, Andrew Mark
 PATENT ASSIGNEE(S): The Council of the Queensland Institute of Medical Research, Australia; Commonwealth Scientific and Industrial Research Organisation; The University of Melbourne; The Walter and Eliza Hall Institute of Medical Research; CSL Ltd.
 SOURCE: PCT Int. Appl., 64 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 9844129</u>	A1	19981008	<u>WO 1998-AU208</u>	19980326
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
<u>CA 2285692</u>	A1	19981008	<u>CA 1998-2285692</u>	19980326
<u>AU 9864902</u>	A	19981022	<u>AU 1998-64902</u>	19980326
<u>AU 728962</u>	B2	20010125		
<u>EP 972054</u>	A1	20000119	<u>EP 1998-910530</u>	19980326
<u>EP 972054</u>	B1	20081210		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
<u>NZ 500151</u>	A	20010126	<u>NZ 1998-500151</u>	19980326
<u>JP 2001522235</u>	T	20011113	<u>JP 1998-540989</u>	19980326
<u>JP 4382163</u>	B2	20091209		
<u>AT 417112</u>	T	20081215	<u>AT 1998-910530</u>	19980326
<u>ZA 9802608</u>	A	19981008	<u>ZA 1998-2608</u>	19980327

<u>US 20030035793</u>	A1	20030220	<u>US 2002-185318</u>	20020628
<u>US 7423016</u>	B2	20080909		
<u>US 20030072742</u>	A1	20030417	<u>US 2002-185799</u>	20020628
<u>US 7423023</u>	B2	20080909		
<u>CA 2489940</u>	A1	20060608	<u>CA 2004-2489940</u>	20041208
<u>PRIORITY APPLN. INFO.:</u>			<u>AU 1997-5891</u>	A 19970327
			<u>AU 1998-1830</u>	A 19980213
			<u>WO 1998-AU208</u>	W 19980326
			<u>US 2000-402020</u>	A1 20000328

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention provides methods of enhancing the immune response to an immunogen and to compns. for use in these methods. In particular the present invention provides a DNA mol. for use in raising an immune response to an antigen. The DNA mol. includes a first sequence encoding a targeting mol., a second sequence encoding the antigen or an epitope thereof, and optionally a third sequence encoding a polypeptide which promotes dimerization or multimerization of the product encoded by the DNA mol. Immunization of mice with a no. of DNA sequences encoding CTLA4-antigen fusions enhanced the immune response to the antigen.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D L18 THIS ABS 1-24

L18 ANSWER 1 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2010:1501342 CAPLUS
DOCUMENT NUMBER: 154:1859
TITLE: Recombinant multiple domain fusion protein mitogens and use thereof for inducing enhancement or repression of antigen-specific immunity
INVENTOR(S): Ochi, Atsuo
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 114pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

<u>PATENT NO.</u>	<u>KIND</u>	<u>DATE</u>	<u>APPLICATION NO.</u>	<u>DATE</u>
-----	----	-----	-----	-----
<u>US 20100303811</u>	A1	20101202	<u>US 2009-483876</u>	20090612
<u>PRIORITY APPLN. INFO.:</u>			<u>US 2008-73010P</u>	P 20080616

AB The invention relates to cell stimulatory fusion proteins and DNA sequences, vectors comprising at least two agonists of TNF/TNFR superfamily, Ig superfamily, cytokine family proteins, and optional antigen combinations. Instructions for use of these proteins and DNA constructs as immune adjuvants and vaccines for treatment of various chronic diseases such as viral infection are also provided. Addnl., the use of these protein and DNA constructs as immune suppressants for treatment of various chronic diseases, such as autoimmunity and organ transplant rejection, is also illustrated. Particularly, this invention provides nucleic acid constructs contg. genes encoding sol. fusion proteins which comprise: (i) a CD40 ligand, a Fas ligand extracellular domain, and an IgG Fc domain; (ii) a CD28 ligand (B7-2), a Fas ligand

extracellular domain, and an IgG Fc domain; (iii) an **OX40** ligand, a **4-1BB** ligand extracellular domain, and an IgG Fc domain; (iv) a CD40 ligand, a ICOS extracellular domain, and an IgG Fc domain; (v) a NGF β ligand, a Fas ligand extracellular domain, and an IgG Fc domain; (vi) an interleukin-2 ligand, a Fas ligand extracellular domain, and an IgG Fc domain. The fusion proteins will preferably elicit a de novo effect to cause immune cell activation relative to when any of the resp. agonistic polypeptides contained therein are administered alone.

L18 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2010:335925 CAPLUS
 DOCUMENT NUMBER: 153:283633
 TITLE: Costimulation signals for memory CD8+ T cells during viral infections
 AUTHOR(S): Duttagupta, Priyanka A.; Boesteanu, Alina C.; Katsikis, Peter D.
 CORPORATE SOURCE: Department of Microbiology and Immunology and Center for Immunology and Vaccine Science, Drexel University College of Medicine, Philadelphia, PA, USA
 SOURCE: Critical Reviews in Immunology (2009), 29(6), 469-486 CODEN: CCRIDE; ISSN: 1040-8401
 PUBLISHER: Begell House, Inc.
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

AB A review. Costimulation signals have been recognized as crit. for optimal T-cell responses and result from important interactions between receptors on the surface of T cells and their ligands on antigen-presenting cells. Two families of receptors, the CD28 family and the tumor necrosis factor receptor (TNFR) family, have been found to be major players in providing costimulation to CD8+ T cells. Recent studies using viral infection models have highlighted the importance of CD28 costimulation signals during memory responses against **viruses**. Programmed death-1 (PD-1), another member of the CD28 family, may contribute to functional defects of helpless memory CD8+ T cells. Members of the TNFR family, such as CD27, **4-1BB**, CD40, TRAIL (tumor necrosis factor-related apoptosis-inducing ligand), and **OX40**, have also been implicated in the survival, generation, maintenance, and quality of **virus**-specific memory CD8+ T cells. The delivery of costimulatory mols. such as CD28, **4-1BB**, and **OX40** can help boost the generation and function of **virus**-specific memory CD8+ T cells. The use of costimulatory mols. as adjuvants, along with viral antigens in vaccines, may facilitate the generation of effective antigen-specific memory CD8+ T-cell responses. Understanding the costimulatory requirements of memory CD8+ T cells, therefore, may lead to improved vaccines that target anti-viral CD8+ T-cell memory.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
 REFERENCE COUNT: 138 THERE ARE 138 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2009:1626269 CAPLUS
 DOCUMENT NUMBER: 152:589804
 TITLE: Expressions of activating and inhibitory receptors as well as costimulatory molecules on peripheral blood natural killer cells in patients with recurrent

genital herpes

AUTHOR(S): Qian, Qifeng; Zhen, Lin; Li, Qing

CORPORATE SOURCE: Center for STD Control and Research, Shenzhen
Institute of Dermatology, Shenzhen, Guangdong
Province, 518020, Peop. Rep. China

SOURCE: Zhonghua Pifuke Zazhi (2009), 42(5), 308-310
CODEN: CHFTAJ; ISSN: 0412-4030

PUBLISHER: Zhongguo Yixue Kexueyuan Pifubing Yanjiuso

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB The expressions of activating receptors (NKG2D and NKp46), inhibitory receptors (NKG2A and KIR) as well as costimulatory mols. (**OX40**, 4-1BB and ICOS) on peripheral blood natural killer (NK) cells from patients with recurrent genital herpes (RGH) were investigated. Four-color immunofluorescence staining with flow cytometry was used to detect the expression of NKG2D, NKG2A, KIR and NKp46 in 44 patients with RGH and 40 normal human controls, and to detect the expressions of **OX40**, 4-1BB and ICOS in 29 patients with RGH and 29 normal human controls. The proportions of NKG2D-pos. and NKp46-pos. NK cells significantly decreased in patients with RGH than those in the normal human controls [(93.3±5.4)% vs. (96.9±2.5)%, (88.9±8.7)% vs. (93.4±4.1)%, resp., both P<0.01]. Between the patients and the controls, no significant difference was obsd. in the expression of NK cell inhibitory receptors, NKG2A [(41.8±14.4)% vs. (46.0 ± 14.7)%, P>0.05] or KIR [(68.3±19.1)% vs. (69.1±17.6)%, P>0.05]. A lower expression of costimulatory mol. **OX40** was noted in NK cells from patients with RGH compared with those in normal controls [(1.0±1.1)% vs. (1.8±1.7)%, P<0.05]. Herpes simplex **virus** infection could down-regulate the expression of NK cell activating receptors and costimulatory mols., subsequently suppress the activation of NK cells, and lead to the escape of **virus**-infected cells from the killing of NK cells.

L18 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2009:1616023 CAPLUS

DOCUMENT NUMBER: 152:104837

TITLE: Therapeutic agents comprising elastin-like peptides
fused to therapeutic proteins for improved
pharmacodynamics

INVENTOR(S): Chilkoti, Ashutosh

PATENT ASSIGNEE(S): Duke University, USA

SOURCE: PCT Int. Appl., 214pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 2009158704</u>	A2	20091230	<u>WO 2009-US49059</u>	20090629
<u>WO 2009158704</u>	A3	20100318		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,
 IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI,
 SK, TR, BF, BJ, BG, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
 TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
 ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

CA 2726894 A1 20091230 CA 2009-2726894 20090629

US 20100022455 A1 20100128 US 2009-493912 20090629

PRIORITY APPLN. INFO.: US 2008-76221P P 20080627

WO 2009-US49059 W 20090629

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 152:104837

AB The present invention provides therapeutic agents and compns. comprising elastin-like peptides (ELPs) and therapeutic proteins. The therapeutic protein may be a glucagon-like peptide-1 (GLP-1) receptor agonist, insulin, or blood-coagulation factor VII/VIIa, including functional analogs. The present invention further provides encoding polynucleotides, as well as methods of making and using the therapeutic agents. The therapeutic agents have improvements in relation to their use as therapeutics, including, inter alia, one or more of half-life, clearance, and/or persistence in the body, soly., and bioavailability. Thus, human factor VII was fused by its C-terminus to ELP1-90, which comprises the VPGXG motif where X is a Val, Gly, or Ala in the ratio 5:3:2 in a 10-unit repeat, repeated 8x with a final C-terminal 10-unit repeat where X is a Val, Gly, Ala, and Cys in the ratio 4:3:2:1. When administered to rats by i.v., factor VII-ELP1-90 demonstrated a half-life of about 690 min, whereas factor VII demonstrated a half-life of 45-50 min.

L18 ANSWER 5 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2009:1556173 CAPLUS

DOCUMENT NUMBER: 153:141678

TITLE: Timing and tuning of CD27-CD70 interactions: the impact of signal strength in setting the balance between adaptive responses and immunopathology

AUTHOR(S): Nolte, Martijn A.; van Olffen, Ronald W.; van Gisbergen, Klaas P. J. M.; van Lier, Rene A. W.

CORPORATE SOURCE: Department of Experimental Immunology, Academic Medical Center, University of Amsterdam, Amsterdam, Neth.

SOURCE: Immunological Reviews (2009), 229(1), 216-231

CODEN: IMRED2; ISSN: 1600-065X

URL: <http://www3.interscience.wiley.com/cgi-bin/fulltext/122341683/PDFSTART>

PUBLISHER: John Wiley & Sons, Inc.

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

AB A review. After binding its natural ligand cluster of differentiation 70 (CD70), CD27, a tumor necrosis factor receptor (TNFR)-assocd. factor-binding member of the TNFR family, regulates cellular activity in subsets of T, B, and natural killer cells as well as hematopoietic progenitor cells. In normal immune responses, CD27 signaling appears to be limited predominantly by the restricted expression of CD70, which is only transiently expressed by cells of the immune system upon activation. Studies performed in CD27-deficient and CD70-transgenic mice have defined a non-redundant role of this receptor-ligand pair in shaping adaptive T-cell responses. Moreover, adjuvant properties of CD70 have been exploited for the design of anti-cancer vaccines. However, continuous CD27-CD70 interactions may cause immune dysregulation and immunopathol. in conditions of chronic immune activation such as during persistent **virus**

infection and autoimmune disease. We conclude that optimal tuning of CD27-CD70 interaction is crucial for the regulation of the cellular immune response. We provide a detailed comparison of costimulation through CD27 with its closely related family members **4-1BB** (GD137), CD30, herpes **virus** entry mediator, **OX40** (CD134), and glucocorticoid-induced TNFR family-related gene, and we argue that these receptors do not have a unique function per se but that rather the timing, context, and intensity of these costimulatory signals det. the functional consequence of their activity.

OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)

REFERENCE COUNT: 144 THERE ARE 144 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2009:839403 CAPLUS

DOCUMENT NUMBER: 151:334741

TITLE: Decreased **4-1BB** expression on HIV-specific CD4+ T cells is associated with sustained viral replication and reduced IL-2 production

AUTHOR(S): Kassu, Afework; D'Souza, Michelle; O'Connor, Brian P.; Kelly-McKnight, Elizabeth; Akkina, Ramesh; Fontenot, Andrew P.; Palmer, Brent E.

CORPORATE SOURCE: Division of Allergy and Clinical Immunology, Department of Medicine, University of Colorado Denver, Aurora, CO, 80045, USA

SOURCE: Clinical Immunology (Amsterdam, Netherlands) (2009), 132(2), 234-245

CODEN: CLIIIFY; ISSN: 1521-6616

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB CD4+ T cell dysfunction in subjects with chronic HIV infection is in part due to an imbalance of costimulatory and coinhibitory receptors. The authors report that **virus**-specific CD4+ T cells expressing **4-1BB** (CD137) or **OX40** (CD134) produced more IL-2 than cells lacking these costimulatory receptors and that **4-1BB** was expressed at a lower level on HIV- than CMV-specific IFN- γ and IL-2 producing CD4+ T cells. Suppression of viral replication with antiretroviral therapy was assocd. with increased **4-1BB** expression on HIV- and CMV-specific IL-2 producing CD4+ T cells and the percentage of IL-2 producing HIV-specific CD4+ T cells that expressed **4-1BB** was inversely correlated with HIV plasma viral load ($r = -0.75$). These findings indicate that the loss of **4-1BB** on HIV-specific CD4+ T cells is assocd. with viral replication and that it may contribute to reduced IL-2 prodn. obsd. during chronic infection.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2007:1114762 CAPLUS

DOCUMENT NUMBER: 147:404820

TITLE: Modulation of immune system components for treatment of respiratory **virus** infections using a composition

comprising a molecular blockade agent to a costimulatory mol.

INVENTOR(S): Hussell, Tracy; Larrick, James W.; Foltin, George L.

PATENT ASSIGNEE(S): Imperial Innovations Limited, UK

SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 2007111931</u>	A2	20071004	<u>WO 2007-US7098</u>	20070322
<u>WO 2007111931</u>	A3	20071129		
<p>W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW</p> <p>RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA</p>				
<u>EP 2010207</u>	A2	20090107	<u>EP 2007-753704</u>	20070322
<p>R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS</p>				
<u>JP 2009530391</u>	T	20090827	<u>JP 2009-501555</u>	20070322
<u>US 20100015143</u>	A1	20100121	<u>US 2009-225459</u>	20090424
<u>PRIORITY APPLN. INFO.:</u>				
			<u>US 2006-785407P</u>	P 20060322
			<u>WO 2007-US7098</u>	W 20070322

AB A compn. comprising a mol. blockade agent to a costimulatory mol. which costimulatory mol. satisfies the following criteria: (1) absent in naive or resting T-lymphocytes; (2). inducible; (3). expressed; and (4). prominent at the height of an immunopathol. response, such as a disease/condition response. Preferably, the costimulatory mol. is **OX40** and the mol. blockade agent is an antibody or antibody fragment having antibody activity to **OX40**. In the examples the inventors use a PEGylated anti-**OX40** antibody (A9) to block the interaction between **OX40** on T cells and **OX40** ligand on antigen-presenting cells in mouse model of respiratory syncytial **virus** and influenza **virus** infection.

L18 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2007:1091580 CAPLUS

DOCUMENT NUMBER: 148:353490

TITLE: Inhibition of **OX40**-Ig on herpetic stromal keratitis in murine model

AUTHOR(S): Xia, Likun; Chen, Xiaolong; Zhu, Yingming; Zhou, Jing

CORPORATE SOURCE: Department of Ophthalmology, Affiliated Second Hospital, China Medical University, Shenyang, 110004, Peop. Rep. China

SOURCE: Yanke Yanjiu (2006), 24(5), 479-483
CODEN: YAYAFH; ISSN: 1003-0808

PUBLISHER: Henan Institute of Ophthalmology

DOCUMENT TYPE: Journal
 LANGUAGE: Chinese

AB Herpetic stromal keratitis (HSK) is an immunoinflammatory lesion in the cornea of the eye set off by the infection with HSV-1. The disease appears to be orchestrated by CD4+ T cells. In current study, it was investigated that the inhibition of **OX40**-Ig on the inhibition of HSK. Corneas of right eyes from 90 BALB/c mice were infected with 106 PFU of HSV-1 McKrae strain. Mice were injected i.p. with **OX40**-Ig or IgG Fc or PBS given on day 0, 2, 4 after the infection. CD4+ T cells from peripheral blood of mice were analyzed on FACS 440 analyzer. The clin. evaluations of infected eyes were taken under the slit-lamp microscope, and the histol. changes of corneas were obsd. under the optical microscope. **Virus** titers in corneas after HSV-1 infection were tested with VERO cells, and delayed type hypersensitivity was obsd. The effects of **OX40**-Ig on HSK were evaluated. As measured by flow cytometry, in the mice treated with **OX40**-Ig, 78.2% of CD4+ T cells were reduced. 83.3% Of the HSV-1-infected control mice developed severe stromal keratitis, but only 20.0% of mice treated by **OX40**-Ig developed HSK. Lesions in **OX40**-Ig treated mice showed markedly reduced severity by slit-lamp microscope, and histol. the corneal stroma had a decrease in inflammatory cell infiltration compared to the control group, and the delayed type hypersensitivity was reduced. The results provide an evidence that blockade of OX-40/OX-40L co-stimulation by **OX40**-Ig can inhibit the proliferation of CD4+ T cells and impair onset and severity of HSK.

L18 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2006:1114150 CAPLUS
 DOCUMENT NUMBER: 146:204173
 TITLE: Anti-**OX40** (CD134) Administration to Nonhuman Primates: immunostimulatory Effects and Toxicokinetic Study
 AUTHOR(S): Weinberg, Andrew D.; Thalhoffer, Colin; Morris, Nick; Walker, Joshua M.; Seiss, Donald; Wong, Scott; Axthelm, Michael K.; Picker, Louis J.; Urba, Walter J.
 CORPORATE SOURCE: Providence Portland Medical Center, Robert W. Franz Cancer Center, Earle A. Chiles Research Institute, Portland, OR, 5F40, USA
 SOURCE: Journal of Immunotherapy (2006), 29(6), 575-585
 CODEN: JOIMF8; ISSN: 1524-9557
 PUBLISHER: Lippincott Williams & Wilkins
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The immune-stimulatory properties of anti-CD134 (**OX40**) antibodies have been well documented in rodents, including their ability to enhance antitumor immunity. In this study, an anti-**OX40** antibody (Ab) known to costimulate monkey T cells in vitro, was infused into rhesus macaque monkeys during immunization with the simian immunodeficiency **virus** protein, gp130. The draining lymph nodes from immunized monkeys treated with anti-**OX40** were enlarged compared with immunized monkeys injected with mouse Ig. Anti-**OX40**-treated monkeys had increased gp130-specific Ab titers, and increased long-lived T-cell responses, compared with controls. There were no overt signs of toxicity in the anti-**OX40**-treated monkeys. The encouraging immune-stimulatory effects led to the good manufg. practice prodn. of an anti-**OX40** Ab for clin. trials in cancer patients. A detailed toxicol. study was performed with anti-**OX40** in nonhuman primates. Three groups of 8 monkeys received anti-**OX40** at 1 of 3 dose levels (0.4, 2.0, and 10 mg/kg) and a control group received saline. No clin. toxicity was obsd., but acute

splenomegaly and enlarged gut-assocd. lymph nodes were obsd. in the anti-**OX40**-treated animals; splenomegaly and lymphadenopathy resolved by day 28. These studies demonstrate the immune-stimulatory properties and safety of anti-**OX40** in primates and provide a strong scientific rationale to pursue clin. trials in humans.

OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2005:1261406 CAPLUS

DOCUMENT NUMBER: 144:18583

TITLE: Cell surface receptor isoforms as modulators of cell surface receptor signaling for treatment of diseases

INVENTOR(S): Jin, Pei; Shepard, Michael H.

PATENT ASSIGNEE(S): Receptor Biologix, Inc., USA

SOURCE: PCT Int. Appl., 654 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 2005113596</u>	A2	20051201	<u>WO 2005-US17051</u>	20050513
<u>WO 2005113596</u>	A3	20070503		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, AP, EA, EP, OA			
<u>AU 2005245896</u>	A1	20051201	<u>AU 2005-245896</u>	20050513
<u>CA 2565974</u>	A1	20051201	<u>CA 2005-2565974</u>	20050513
<u>US 20060286102</u>	A1	20061221	<u>US 2005-129740</u>	20050513
<u>EP 1745073</u>	A2	20070124	<u>EP 2005-752088</u>	20050513
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU			
<u>JP 2008506366</u>	T	20080306	<u>JP 2007-513460</u>	20050513
<u>US 20090170769</u>	A1	20090702	<u>US 2008-260961</u>	20081029
<u>PRIORITY APPLN. INFO.:</u>			<u>US 2004-571289P</u>	P 20040514
			<u>US 2004-580990P</u>	P 20040618
			<u>US 2005-666825P</u>	P 20050330
			<u>US 2005-129740</u>	B1 20050513
			<u>WO 2005-US17051</u>	W 20050513

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Isoforms of cell surface receptors, including isoforms of receptor tyrosine kinases and pharmaceutical compns. contg. receptor tyrosine kinase isoforms are provided. Chimeras and conjugates contg. the cell

surface receptors which contain a portion, such as an extracellular domain, from one cell surface receptor and a second portion, particularly an intron-encoded portion, from a second cell surface protein, also are provided. The isoforms modulate the activity of a cell surface receptor. Methods for identifying and prep. isoforms of cell surface receptors including receptor tyrosine kinases are provided. Also provided are methods of disease treatment with the cell surface receptor isoforms.

L18 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2005:631071 CAPLUS
 DOCUMENT NUMBER: 143:171256
 TITLE: During Viral Infection of the Respiratory Tract, CD27, 4-1BB, and OX40 Collectively Determine Formation of CD8+ Memory T Cells and Their Capacity for Secondary Expansion
 AUTHOR(S): Hendriks, Jenny; Xiao, Yanling; Rossen, John W. A.; van der Sluijs, Koenraad F.; Sugamura, Kazuo; Ishii, Naoto; Borst, Jannie
 CORPORATE SOURCE: Division of Immunology, Netherlands Cancer Institute, Amsterdam, Neth.
 SOURCE: Journal of Immunology (2005), 175(3), 1665-1676
 CODEN: JOIMA3; ISSN: 0022-1767
 PUBLISHER: American Association of Immunologists
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Independent studies have shown that CD27, 4-1BB, and OX40 can all promote survival of activated CD8+ T cells. The authors have therefore compared their impact on CD8+ memory T cell formation and responsiveness within one, physiol. relevant model system. Recombinant mice, selectively lacking input of one or two receptors, were challenged intranasally with influenza virus, and the immunodominant virus-specific CD8+ T cell response was quantified at priming and effector sites. Upon primary infection, CD27 and (to a lesser extent) 4-1BB made nonredundant contributions to accumulation of CD8+ virus-specific T cells in draining lymph nodes and lung, while OX40 had no effect. Interestingly though, in the memory response, accumulation of virus-specific CD8+ T cells in spleen and lung critically depended on all three receptor systems. This was explained by two observations: 1) CD27, 4-1BB, and OX40 were collectively responsible for generation of the same memory CD8+ T cell pool; 2) CD27, 4-1BB, and OX40 collectively detd. the extent of secondary expansion, as shown by adoptive transfers with standardized nos. of memory cells. Surprisingly, wild-type CD8+ memory T cells expanded normally in primed OX40 ligand- or 4-1BB ligand-deficient mice. However, when wild-type memory cells were generated in OX40 ligand- or 4-1BB ligand-deficient mice, their secondary expansion was impaired. This provides the novel concept that stimulation of CD8+ T cells by OX40 and 4-1BB ligand during priming imprints into them the capacity for secondary expansion. The authors' data argue that ligand on dendritic cells and/or B cells may be crit. for this.

OS.CITING REF COUNT: 75 THERE ARE 75 CAPLUS RECORDS THAT CITE THIS RECORD (75 CITINGS)
 REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2005:117708 CAPLUS

DOCUMENT NUMBER: 142:196145
 TITLE: Potential immunogenicity of adult T cell leukemia cells in vivo
 AUTHOR(S): Kurihara, Kiyoshi; Harashima, Nanae; Hanabuchi, Shino; Masuda, Masato; Utsunomiya, Atae; Tanosaki, Ryuji; Tomonaga, Masao; Ohashi, Takashi; Hasegawa, Atsuhiko; Masuda, Takao; Okamura, Jun; Tanaka, Yuetsu; Kannagi, Mari
 CORPORATE SOURCE: Department of Immunotherapeutics, Graduate School, Tokyo Medical and Dental University, Tokyo, 113-8519, Japan
 SOURCE: International Journal of Cancer (2005), 114(2), 257-267
 CODEN: IJCNAW; ISSN: 0020-7136
 PUBLISHER: Wiley-Liss, Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Exptl. vaccines targeting human T cell leukemia **virus** type-I (HTLV-I) Tax have been demonstrated in a rat model of HTLV-I-induced lymphomas. However, the scarcity of HTLV-I-expression and the presence of defective HTLV-I-proviruses in adult T cell leukemia (ATL) cells have raised controversy about the therapeutic potential of HTLV-I-targeted immunotherapy in humans. The authors investigated the expression of HTLV-I antigens in fresh ATL cells by using both in vitro and in vivo assays. In flow cytometric anal., the authors found that 3 of 5 acute-type and six of fifteen chronic-type ATL patients tested showed significant induction of HTLV-I Tax and Gag in their ATL cells in a 1-day culture. Concomitantly with HTLV-I-expression, these ATL cells expressed co-stimulatory mols. such as CD80, CD86 and **Ox40**, and showed elevated levels of antigenicity against allogeneic T cells and HTLV-I Tax-specific cytotoxic T-lymphocytes (CTL). Representative CTL epitopes restricted by HLA-A2 or A24 were conserved in 4 of 5 acute-type ATL patients tested. Furthermore, spleen T cells from rats, which had been s.c. inoculated with formalin-fixed uncultured ATL cells, exhibited a strong interferon gamma-producing helper T cell responses specific for HTLV-I Tax-expressing cells. This study indicates that ATL cells from about half the patients tested readily express HTLV-I antigens including Tax in vitro, and that ATL cells express sufficient amts. of Tax or Tax-induced antigens to evoke specific T cell responses in vivo.

OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2004:706197 CAPLUS
 DOCUMENT NUMBER: 141:348613
 TITLE: Factors that increase the effective concentration of CXCR4 dictate feline immunodeficiency **virus** tropism and kinetics of replication
 AUTHOR(S): de Parseval, Aymeric; Ngo, Stacie; Sun, Peiqing; Elder, John H.
 CORPORATE SOURCE: Department of Molecular Biology, The Scripps Research Institute, La Jolla, CA, USA
 SOURCE: Journal of Virology (2004), 78(17), 9132-9143
 CODEN: JOVIAM; ISSN: 0022-538X
 PUBLISHER: American Society for Microbiology
 DOCUMENT TYPE: Journal

LANGUAGE: English

AB The surface glycoprotein (gp95) of the feline immunodeficiency **virus** (FIV) binds in a strain-specific manner to several cell surface mols., including CXCR4, heparan sulfate proteoglycans (HSPGs), DC-SIGN, and a 43-kDa cell surface receptor on T cells recently identified as CD134 by M. Shimojima et al. CXCR4 is the entry receptor in all known cases, and the other mols. act as binding receptors to help facilitate infection. In this report, the authors confirm and extend the findings regarding CD134 as a primary receptor for FIV. In addn., the authors show that temp. critically influences the binding properties of FIV gp95 to CXCR4 and HSPGs. The data show that gp95 of the field strain FIV-PPR bound to CXCR4 at 22°, whereas binding was not detected at 4°. In contrast, binding of the lab. adapted FIV-34TF10 gp95 was obsd. at either 4° or 22°, albeit at increased levels at the higher temp. The level of CXCR4 increased after the temp. was switched from 4 to 22°, whereas the level of HSPGs decreased, resulting in higher binding of gp95 from both strains to CXCR4 and lower binding of gp95 of FIV-34TF10 to HSPGs (FIV-PPR gp95 does not bind to these mols.). The findings also show that HSPGs facilitate the CXCR4-mediated infectivity of CrFK and G355-5 cells by FIV-34TF10. These two nonlymphoid cell lines express very low levels of CXCR4 and are permissive to FIV-34TF10 but not to productive infection by FIV-PPR. However, overexpression of human CXCR4 in CrFK or G-355-5 cells resulted in extensive cell fusion and infection by FIV-PPR. Taken together, these findings indicate that factors that increase the effective concn. of CXCR4 enhance FIV infectivity and may involve (i) temp. or ligand-induced conformational changes in CXCR4 that enhance SU binding, (ii) coreceptor interactions with gp95 that either alter gp95 conformation to enhance CXCR4 binding and/or raise the localized concn. of receptor or ligand, or (iii) direct increase in CXCR4 concn. via overexpression.

OS.CITING REF COUNT: 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS RECORD (20 CITINGS)

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2004:676377 CAPLUS

DOCUMENT NUMBER: 141:312868

TITLE: **4**-1BB and **OX40** stimulation enhance CD8 and CD4 T-cell responses to a DNA prime, poxvirus boost vaccine

AUTHOR(S): Munks, Michael W.; Mourich, Dan V.; Mittler, Robert S.; Weinberg, Andrew D.; Hill, Ann B.

CORPORATE SOURCE: Department of Molecular Microbiology and Immunology, Oregon Health and Science University, Portland, OR, USA

SOURCE: Immunology (2004), 112(4), 559-566

CODEN: IMMUAM; ISSN: 0019-2805

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **4**-1BB (CD137) is a tumor necrosis factor receptor (TNFR) family member, expressed primarily on CD8 T cells after activation. Signaling through **4**-1BB has been reported to enhance CD8 T-cell expansion and to protect activated CD8 T cells from death, resulting in an enlarged memory population. Although stimulating **4**-1BB has been shown to significantly improve the immune response to weak immunogens such as tumors, little is known about its effect on the CD8 T-cell response to a powerful viral

vector such as vaccinia. To test 4-1BB's ability to improve the murine CD8 T cell response to a DNA prime, poxvirus boost vaccine, similar to those used for human immunodeficiency **virus** and simian immunodeficiency **virus** vaccines, we administered 4-1BB agonist antibody at the time of the poxvirus boost. 4-1BB stimulation increased the no. of functional memory CD8 T cells by two- to fourfold. However, we saw a similar enhancement at the peak of the response and in the memory phase, thus we found no evidence in the context of **virus** infection that 4-1BB stimulation could increase the percentage of CD8 T cells that survive the acute activation phase to become memory cells. **OX40** (CD134) is an analogous TNFR family member expressed primarily on activated CD4 T cells. **OX40** stimulation increased the no. of antigen-specific CD4 T cells approx. threefold. Stimulating both 4-1BB and **OX40** enhanced the CD8 T-cell response more than 4-1BB alone. Thus stimulating these receptors can improve the response to a powerful **virus** vector, and may be useful in vaccine development.

OS.CITING REF COUNT: 21 THERE ARE 21 CAPLUS RECORDS THAT CITE THIS RECORD (21 CITINGS)
 REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2004:644847 CAPLUS
 DOCUMENT NUMBER: 141:422914
 TITLE: Co-stimulation: novel methods for preventing viral-induced lung inflammation
 AUTHOR(S): Hussell, Tracy; Snelgrove, Robert; Humphreys, Ian R.; Williams, Andrew E.
 CORPORATE SOURCE: Centre for Molecular Microbiology and Infection, Technology and Medicine, Imperial College of Science, London, SW7 2AZ, UK
 SOURCE: Trends in Molecular Medicine (2004), 10(8), 379-386
 CODEN: TMMRCY; ISSN: 1471-4914
 PUBLISHER: Elsevier Ltd.
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

AB A review. Respiratory infections cause significant morbidity and mortality worldwide. Although an immune response is required to eliminate respiratory pathogens, if unchecked, it can damage surrounding tissues and block primary lung function. Based on our knowledge of immune T-cell activation, there are several pathways to which immune intervention could be applied. However, relatively few interventions target only those immune cells that are responding to antigens. **OX40** and 4-1BB are members of the tumor necrosis factor receptor family and are expressed on the surface of T cells in several inflammatory conditions. Recently, the inhibition of **OX40** has proved beneficial during influenza **virus** infection. This review highlights the recent advances in the manipulation of such mols. and how they have been applied to inflammatory conditions that are caused by **viruses** in the lung.

OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
 REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2004:589386 CAPLUS

DOCUMENT NUMBER: 141:139130
 TITLE: Vaccines comprising TLR agonist, TNF/TNF receptor agonist and antigen for inducing cellular immune response against infection or tumor
 INVENTOR(S): Noelle, Randolph J.; Ahonen, Cory L.; Kedl, Ross M.
 PATENT ASSIGNEE(S): 3M Innovative Properties Company, USA
 SOURCE: PCT Int. Appl., 48 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 2004060319</u>	A2	20040722	<u>WO 2003-US41796</u>	20031230
<u>WO 2004060319</u>	A3	20041104		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
<u>CA 2511538</u>	A1	20040722	<u>CA 2003-2511538</u>	20031230
<u>US 20040141950</u>	A1	20040722	<u>US 2003-748010</u>	20031230
<u>US 7387271</u>	B2	20080617		
<u>AU 2003300184</u>	A1	20040729	<u>AU 2003-300184</u>	20031230
<u>AU 2003300184</u>	B2	20090806		
<u>EP 1578419</u>	A2	20050928	<u>EP 2003-800433</u>	20031230
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
<u>JP 2006512391</u>	T	20060413	<u>JP 2004-564947</u>	20031230
<u>US 20090123460</u>	A1	20090514	<u>US 2008-49874</u>	20080317
<u>US 20110002946</u>	A1	20110106	<u>US 2010-845888</u>	20100729
<u>JP 2011016811</u>	A	20110127	<u>JP 2010-181794</u>	20100816
PRIORITY APPLN. INFO.:			<u>US 2002-437398P</u>	P 20021230
			<u>JP 2004-564947</u>	A3 20031230
			<u>US 2003-748010</u>	A3 20031230
			<u>WO 2003-US41796</u>	W 20031230
			<u>US 2008-49874</u>	A3 20080317

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention provides immunostimulatory combinations. Generally, the immunostimulatory combinations include a TLR agonist, a TNF or TNF receptor agonist and an tumor antigen or viral, bacterial or parasitic antigen. The TLR agonist is an agonist of TLR1-10 e.g. IRM compd., MALP-2, LPS, polyIC, CpG or any combination. The TNF agonist is an agonist or antibody against CD40L, **OX40** ligand, **4-1BB** ligand, CD27, CD30 ligand, TNF- α , TNF- β , RANK ligand, LT- α , LT- β , GITR ligand or LIGHT. The TNF receptor agonist is an antibody or agonist of CD40, **OX40**, **4-1BB**, CD27 ligand, CD30, TNFR2, RANK, LT- α R, LT- β R, HVEM, GITR, TROY or RELT. These immunostimulatory combinations are useful for inducing Th1 immune response or antigen-specific CD8+ effector and memory T cell response against infectious and neoplastic conditions.

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2003:709813 CAPLUS
 DOCUMENT NUMBER: 139:212497
 TITLE: Co-stimulatory members of the TNFR family: Keys to effective T-cell immunity?
 AUTHOR(S): Croft, Michael
 CORPORATE SOURCE: Division of Molecular Immunology, La Jolla, Institute for Allergy and Immunology, San Diego, CA, 92121, USA
 SOURCE: Nature Reviews Immunology (2003), 3(8), 609-620
 CODEN: NRIABX; ISSN: 1474-1733
 PUBLISHER: Nature Publishing Group
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

AB A review. Interactions between co-stimulatory ligands and their receptors are crucial for the activation of T cells, the prevention of tolerance and the development of T-cell immunity. It is now evident that members of the Ig-like CD28-B7 co-stimulatory family cannot fully account for an effective long-lasting T-cell response or the generation of memory T cells. Several members of the tumor-necrosis factor receptor (TNFR) superfamily - **OX40**, **4-1BB**, CD27, CD30 and HVEM (herpes-**virus** entry mediator) - are poised to deliver co-stimulatory signals both early and late after encounter with antigen. The roles of these mols. in initiating and sustaining the T-cell response and in promoting long-lived immunity are discussed.

OS.CITING REF COUNT: 369 THERE ARE 369 CAPLUS RECORDS THAT CITE THIS RECORD (370 CITINGS)

REFERENCE COUNT: 130 THERE ARE 130 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2003:408183 CAPLUS
 DOCUMENT NUMBER: 139:5231
 TITLE: Autoimmune chronic inflammatory arthropathy in mice transgenic for the HTLV-I tax gene
 AUTHOR(S): Iwakura, Yoichiro
 CORPORATE SOURCE: Center for Experimental Medicine, Institute of Medical Science, University of Tokyo, Minato-ku, Tokyo, 108-8639, Japan
 SOURCE: Gann Monograph on Cancer Research (2003), 50(Two Decades of Adult T-Cell Leukemia and HTLV-1 Research), 197-218
 CODEN: GMCRCDC; ISSN: 0072-0151
 PUBLISHER: Japan Scientific Societies Press
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

AB A review. Rheumatoid arthritis (RA) is a serious medical problem, with 1% of the people in the world affected. The disease is autoimmune in nature and characterized by chronic inflammation of the synovial tissue in multiple joints, which leads to joint destruction. It is remarkable that expression of inflammatory cytokines is augmented in the joints of the patients, although the pathol. roles have not been elucidated completely. The authors recently reported on an inflammatory arthropathy

resembling RA that develops in high incidence among transgenic (Tg) mice that carry the env-pX region of the human T cell leukemia **virus** type I (HTLV-I) genome. Autoimmune pathogenesis was suggested in this RA model because: (1) high levels of autoantibodies were detected in the serum, (2) oligoclonal accumulation of T cells was detected in the affected joints, (3) the development of arthritis was suppressed in athymic nude mice, and (4) the disease was transferred by bone-marrow (BM) cell transplantation and suppressed by wild-type BM cell transplantation. The authors found that cytokine levels including interleukin (IL)-1 were elevated in the joints of these Tg mice. Depletion of IL-1 by gene targeting greatly reduced onset of the disease and T cell proliferative response against synovial components was also reduced, indicating importance of this cytokine in the development of arthritis and autoimmunity. Furthermore, the authors found that IL-1 receptor antagonist (IL-1Ra)-deficient mice also developed arthritis spontaneously, and autoimmune nature of the disease was suggested. These observations suggest that excess IL-1 signal causes autoimmunity. The authors show that IL-1 induces expression on T cells of CD40L and **OX40** co-signaling mols., which play important roles in T cell-antigen presenting cell interaction, and activate the immune system non-specifically. In this review, I will discuss pathogenic roles of Tax-induced IL-1 in the development of autoimmunity and arthritis in mouse models.

REFERENCE COUNT: 140 THERE ARE 140 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2002:353295 CAPLUS
 DOCUMENT NUMBER: 136:368437
 TITLE: Agents inducing mobilization, maturation, and activation of dendritic cells and T cell-enhancing factor are used for treating infection
 INVENTOR(S): Lynch, David H.; De Smedt, Thibaut N.; Maliszewski, Charles R.; Butz, Eric A.; Miller, Robert E.; Thomas, Elaine K.
 PATENT ASSIGNEE(S): Immunex Corporation, USA
 SOURCE: PCT Int. Appl., 43 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002036141	A2	20020510	WO 2001-US44834	20011030
WO 2002036141	A3	20030821		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2002032447	A5	20020515	AU 2002-32447	20011030

US 20040247563 A1 20041209 US 2004-399116 20040527
 PRIORITY APPLN. INFO.: US 2000-245721P P 20001102
 WO 2001-US44834 W 20011030

AB An improved method for treatment of an individual suffering from or at risk for an infectious disease, comprising administering to said individual a combination of from two to five agents is disclosed. The agents may be agents (e.g. Flt3L) that mobilize dendritic cells, agents (e.g. TRAIL) that cause death or growth inhibition of infectious agents, chemoattractants, agents (e.g. CD40L) that stimulate maturation of dendritic cells, and agents (e.g. IL-15, OX40 agonist, 4-1BB agonist) that enhance an immune response of an effector T cell. Antigen-expressing, activated dendritic cells are disclosed. Such dendritic cells are used to present antigens (specifically, antigens derived from infectious agents) to T cells, and can be useful in vaccination protocols. Useful cytokines can be used in sep., sequential or simultaneous combination with the activated, antigen-pulsed dendritic cells. Also disclosed are methods for stimulating an immune response using the antigen-expressing, activated dendritic cells.

OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN

Full Text Reference

ACCESSION NUMBER: 2001:809019 CAPLUS
 DOCUMENT NUMBER: 135:343303
 TITLE: Method for enhancing an antigen specific immune response with OX-40 ligand
 INVENTOR(S): Weinberg, Andrew D.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S., 30 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6312700	B1	20011106	US 1999-255363	19990223
US 20020054873	A1	20020509	US 2001-946832	20010904
US 7504101	B2	20090317		
US 20070207159	A1	20070906	US 2006-529956	20060929
US 7622444	B2	20091124		

PRIORITY APPLN. INFO.: US 1998-75801P P 19980224
 US 1999-255363 A3 19990223
 US 2001-946832 A1 20010904

AB Provided are compns. and methods for enhancing the immune response of a mammal to an antigen by engaging the OX-40 receptor on the surface of T-cells are disclosed, comprising administering to the mammal a compn. comprising a purified OX-40 receptor binding agent and a pharmaceutically acceptable carrier, wherein said compn. is administered to the mammal such that the OX-40 receptor binding agent is presented to T-cells of the mammal during or shortly after priming of the T-cells by the antigen. Such compns. and methods can be used in immunization and cancer treatment.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2000:569685 CAPLUS
 DOCUMENT NUMBER: 133:262877
 TITLE: Thermodynamic characterization of the interaction between TRAF2 and tumor necrosis factor receptor peptides by isothermal titration calorimetry
 AUTHOR(S): Ye, Hong; Wu, Hao
 CORPORATE SOURCE: Department of Biochemistry, Weill Medical College of Cornell University, New York, NY, 10021, USA
 SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(16), 8961-8966
 CODEN: PNASA6; ISSN: 0027-8424
 PUBLISHER: National Academy of Sciences
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The tumor necrosis factor receptor (TNFR) superfamily can induce diverse biol. effects, including cell survival, proliferation, differentiation, and apoptosis. The major signal transducers for TNFRs are the family of TNF receptor assocd. factors (TRAFs). The direct interaction between TRAFs and the intracellular tails of TNFRs is the first step of this signal relay process. Structural studies have revealed a trimeric nature of TRAF2 and a sym. mode of receptor binding, suggesting the involvement of trivalent TNFR2-receptor interaction in the signal transduction. In this study, using isothermal titrn. calorimetry (ITC), we report thermodyn. characterization of the interaction between TRAF2 and monomeric peptide sequences from TNFR members, including TNFR2, CD40, CD30, ~~Ox~~40, and 4-1BB, and the Epstein-Barr **virus** (EBV)-transforming protein, latent infection membrane protein-1 (LMP1). The dissocn. consts. of the interaction were shown to range between 40 μ M and 1.9 mM, which are substantially weaker than most protein-peptide interactions. The interaction is entirely driven by exothermic enthalpy, consistent with the abundance of polar contacts. The enthalpy of the interaction has a significant temp. dependence ($\Delta C_p = -245$ cal/mol \cdot K). The unfavorable entropy in the interaction and the comparison with structural energetics calcns. suggest the involvement of conformational rearrangement in the interaction. The low affinity of TRAF2 to monomeric receptor peptides further supports the importance of avidity contribution in TRAF2 recruitment by these receptors upon ligand-induced trimerization or higher order oligomerization.

OS.CITING REF COUNT: 38 THERE ARE 38 CAPLUS RECORDS THAT CITE THIS RECORD (38 CITINGS)
 REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2000:488672 CAPLUS
 DOCUMENT NUMBER: 133:191620
 TITLE: Costimulation in antiviral immunity: differential requirements for CD4+ and CD8+ T cell responses
 AUTHOR(S): Whitmire, Jason K.; Ahmed, Rafi
 CORPORATE SOURCE: Department of Molecular Immunology, La Jolla Institute for Allergy and Immunology, San Diego, CA, 92121, USA
 SOURCE: Current Opinion in Immunology (2000), 12(4), 448-455
 CODEN: COPIEL; ISSN: 0952-7915

PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

AB A review and discussion with 58 refs. A key step toward improving vaccines is understanding the mol. interactions responsible for inducing antiviral T cell responses. An emerging theme from recent studies is that CD4+ and CD8+ T cell responses require distinct costimulatory pathways for activation. In addn., these costimulatory interactions can play a crucial role during the death phase of the T cell response and det. the no. of effector T cells that survive to become memory T cells.

OS.CITING REF COUNT: 94 THERE ARE 94 CAPLUS RECORDS THAT CITE THIS RECORD (94 CITINGS)

REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 1998:684978 CAPLUS

DOCUMENT NUMBER: 129:274700

ORIGINAL REFERENCE NO.: 129:56017a,56020a

TITLE: DNA encoding targeting protein fused to antigen or epitope in enhancement of immune response to DNA vaccines

INVENTOR(S): Boyle, Jefferey Stephen; Brady, Jamie Louise; Lew, Andrew Mark

PATENT ASSIGNEE(S): The Council of the Queensland Institute of Medical Research, Australia; Commonwealth Scientific and Industrial Research Organisation; The University of Melbourne; The Walter and Eliza Hall Institute of Medical Research; CSL Ltd.

SOURCE: PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 9844129</u>	A1	19981008	<u>WO 1998-AU208</u>	19980326
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
<u>CA 2285692</u>	A1	19981008	<u>CA 1998-2285692</u>	19980326
<u>AU 9864902</u>	A	19981022	<u>AU 1998-64902</u>	19980326
<u>AU 728962</u>	B2	20010125		
<u>EP 972054</u>	A1	20000119	<u>EP 1998-910530</u>	19980326
<u>EP 972054</u>	B1	20081210		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
<u>NZ 500151</u>	A	20010126	<u>NZ 1998-500151</u>	19980326
<u>JP 2001522235</u>	T	20011113	<u>JP 1998-540989</u>	19980326
<u>JP 4382163</u>	B2	20091209		
<u>AT 417112</u>	T	20081215	<u>AT 1998-910530</u>	19980326

<u>ZA 9802608</u>	A	19981008	<u>ZA 1998-2608</u>	19980327
<u>US 20030035793</u>	A1	20030220	<u>US 2002-185318</u>	20020628
<u>US 7423016</u>	B2	20080909		
<u>US 20030072742</u>	A1	20030417	<u>US 2002-185799</u>	20020628
<u>US 7423023</u>	B2	20080909		
<u>CA 2489940</u>	A1	20060608	<u>CA 2004-2489940</u>	20041208
PRIORITY APPLN. INFO.:			<u>AU 1997-5891</u>	A 19970327
			<u>AU 1998-1830</u>	A 19980213
			<u>WO 1998-AU208</u>	W 19980326
			<u>US 2000-402020</u>	A1 20000328

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention provides methods of enhancing the immune response to an immunogen and to compns. for use in these methods. In particular the present invention provides a DNA mol. for use in raising an immune response to an antigen. The DNA mol. includes a first sequence encoding a targeting mol., a second sequence encoding the antigen or an epitope thereof, and optionally a third sequence encoding a polypeptide which promotes dimerization or multimerization of the product encoded by the DNA mol. Immunization of mice with a no. of DNA sequences encoding CTLA4-antigen fusions enhanced the immune response to the antigen.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 1994:698641 CAPLUS
DOCUMENT NUMBER: 121:298641
ORIGINAL REFERENCE NO.: 121:54643a,54646a
TITLE: Molecular characterization of murine and human **OX40**/**OX40** ligand systems: identification of a human **OX40** ligand as the HTLV-1-regulated protein gp34
AUTHOR(S): Baum, Peter R.; Gayle, Richard B., III; Ramsdell, Fred; Srinivasan, Subhashini; Sorensen, Rick A.; Watson, Mark L.; Seldin, Michael F.; Baker, Elizabeth; Sutherland, Grant R.; et al.
CORPORATE SOURCE: Dep. Gene Expression, Immunex R&D Corporation, Seattle, WA, 98101, USA
SOURCE: EMBO Journal (1994), 13(17), 3992-4001
CODEN: EMJODG; ISSN: 0261-4189
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A ligand was cloned for murine **OX40**, a member of the TNF receptor family, using a T cell lymphoma cDNA library. The ligand (muOX40L) is a type II membrane protein with significant identity to human gp34 (gp34), a protein whose expression on HTLV-1-infected human leukemic T cells is regulated by the tax gene. The predicted structures of muOX40L and gp34 are similar to, but more compact than, those of other ligands of the TNF family. Mapping of the muOX40L gene revealed tight linkage to gld, the FasL gene, on chromosome 1. Gp34 maps to a homologous region in the human genome, 1q25. CDNAs for human **OX40** receptor were cloned by cross-hybridization with muOX40, and gp34 was found to bind the expressed human receptor. Lymphoid expression of muOX40L was detected on activated T cells, with higher levels found on CD4+ rather than CD8+ cells. The cell-bound recombinant ligands are biol. active, co-stimulating T cell proliferation and cytokine prodn. Strong induction of IL-4 secretion by muOX40L suggests that this ligand may play a role in regulating immune responses. In addn., the HTLV-1 regulation of gp34 suggests a possible

connection between virally induced pathogenesis and the **OX40** system.
 OS.CITING REF COUNT: 170 THERE ARE 170 CAPLUS RECORDS THAT CITE THIS
 RECORD (172 CITINGS)

=> D L16 IBIB ABS 1-24

L16 ANSWER 1 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2010:1563248 CAPLUS
 TITLE: Study on expression of natural killer (NK) cell C-type
 lectin-like receptors in nasal NK/T-cell lymphomas
 AUTHOR(S): Nong, Lin; Zhang, Shuang; Li, Yang; Zhang, Ying; Wang,
 Ying; Li, Ting
 CORPORATE SOURCE: Department of Pathology, First Hospital, Peking
 University, Beijing, 100034, Peop. Rep. China
 SOURCE: Zhonghua Binglixue Zazhi (2010), 39(5), 319-324
 CODEN: CHPLAB; ISSN: 0529-5807
 PUBLISHER: Zhonghua Yixuehui Zazhishe
 DOCUMENT TYPE: Journal
 LANGUAGE: Chinese

AB The aim of this paper is to investigate the expression and possible role
 of C-type lectin-like natural killer cell receptors, including CD94 and
 NKG2s, in extranodal NK/T-cell lymphoma, nasal type (EN-NK/T-NT). Reverse
 transcriptase polymerase chain reaction (RT-PCR) was used to detect the
 expression of CD94 and NKG2s in tissue sections of 21 cases of EN-NK/T-NT
 (confirmed by histol., immunohistochem., in-situ hybridization for
 Epstein-Barr virus (EBV) and PCR for T-cell receptor genes), eight midline
 B cell lymphomas (BCL), 10 peripheral T cell lymphoma of lymph nodes
 (PTCL), five spleens, five thymuses and five chronic nasopharyngitis. All
 21 cases of EN-NK/T-NT showed typical histol. features, with expression of
 CD38, CD56, cytotoxic granules and positivity of EBV in 20 cases. The
 RT-PCR results showed a high level expression of CD94 (85.7%) and **NKG2**
 members (95.2% totally, with NKG2A/2B in 85.7%, NKG2D in 61.9%, NKG2F in
 14.3%, NKG2C/2E in 4.8%, resp. and sequentially) in EN-NK/T-NT. But
 in the controls, none of the receptors were detected in TCL(0%) and
 BCL(0%), while only a few cases of lymphoid tissues expressed one or two
 of these receptors (two spleens and two chronic nasopharyngitis mucosa for
 CD94, one spleen for NKG2A/2B and one thymus for NKG2D). The differences
 of CD94 and **NKG2** expression between EN-NK/T-NT and BCL or TCL were
 statistically significant ($P < 0.01$). Co-expression of CD94 and **NKG2** was
 found in 17 out of 21 EN-NK/T-NT cases (81.0%). The specific and
 sequential expression nature of CD94 and **NKG2** in EN-NK/T-NT, mimicks the
 developmental expression model in their normal counterparts, and suggests
 that the tumor cells of most cases are being activated and keeping in a
 stage as the functional NK cells. Detection of these mols. may provide a
 useful tool to confirm the diagnosis of NK cell lymphoma.

L16 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2009:729195 CAPLUS
 DOCUMENT NUMBER: 151:116781
 TITLE: 17 β -Estradiol enhances interleukin-18 mRNA
 expression after sensitization of mice with contact
 hypersensitivity
 AUTHOR(S): Sakazaki, Fumitoshi; Fujiyama, Masahiro; Ueno,
 Hitoshi; Nagase, Hisamitsu; Nakamuro, Katsuhiko
 CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Setsunan

SOURCE: University, Hirakata, 573-0101, Japan
 Journal of Health Science (2009), 55(3), 396-404
 CODEN: JHSCFD; ISSN: 1344-9702
 PUBLISHER: Pharmaceutical Society of Japan
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB To clarify the mechanism underlying the enhancing effect of 17 β -estradiol (E2) on contact hypersensitivity (CHS) and the expression of interferon (IFN)- γ in mice, the mRNA expression levels of interleukin (IL)-18 were evaluated. Female BALB/c mice aged 3 wk were ovariectomized, administered 3.2 μ g of E2, and sensitized by 50 μ L of 3% 4-ethoxymethylene-2-phenyl-2-oxazolin-one (OXA). Seven days later, CHS was elicited by the application of 7.5 μ L of 1% OXA on the ear auricles. The auricles, cervical lymph nodes and spleens were excised, and gene expression was evaluated by reverse transcription-polymerase chain reaction. E2 enhanced the expression of IL-18 mRNA in the spleen on the following day and in the ear auricles on days 4 and 7 after sensitization with OXA. The preadministration of an antibody against IL-18 receptor suppressed the CHS and reduced IFN- γ mRNA expression in E2-administered mice. IL-18 was present in the dermis of the ear skin and absent in the epidermis. E2 also enhanced the expression of IFN- γ and IL-18 mRNAs in splenocytes cultured with lipopolysaccharide (LPS). IL-18 protein was detected by flow cytometry in CD4+, CD8+ and **NKG2+** lymphocytes among splenocytes cultured with LPS. These results suggest that E2 enhances lymphocyte activation in the sensitization phase of CHS, and that IFN- γ mRNA expression is enhanced in the elicitation phase of CHS.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
 (1 CITINGS)

L16 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2009:645108 CAPLUS
 DOCUMENT NUMBER: 153:404068
 TITLE: Breast cancer cells expressing stem cell markers CD44+ CD24lo are eliminated by Numb-1 peptide-activated T cells
 AUTHOR(S): Mine, Takashi; Matsueda, Satoko; Li, Yufeng; Tokumitsu, Hiroshi; Gao, Hui; Danes, Cristopher; Wong, Kwong-Kwok; Wang, Xinhui; Ferrone, Soldano; Ioannides, Constantin G.
 CORPORATE SOURCE: Department of Gynecologic Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
 SOURCE: Cancer Immunology Immunotherapy (2009), 58(8), 1185-1194
 CODEN: CIIMDN; ISSN: 0340-7004
 PUBLISHER: Springer
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Cancer stem cells (CSC) are resistant to chemo- and radiotherapy. To eliminate cells with phenotypic markers of CSC-like we characterized: (1) expression of CD44, CD24, CD133 and MIC-A/B (**NKG2** receptors) in breast (MCF7) and ovarian (SK-OV-3) cells resistant to gemcitabine (GEM), paclitaxel (PTX) and 5-fluorouracil (5-FU) and (2) their elimination by Numb- and Notch-peptide activated CTL. The no. of cells in all populations with the luminal CSC phenotype [epithelial specific antigen+ (ESA) CD44hi CD24lo, CD44hi CD133+, and CD133+ CD24lo] increased in drug-resistant MCF7 and SK-OV-3 cells. Similarly, the no. of cells with

expressed MIC-A/B increased 4 times in drug-resistant tumor cells compared with drug-sensitive cells. GEMRes MCF7 cells had lower levels of the Notch-1-extracellular domain (NECD) and Notch trans-membrane intracellular domain (TMIC) than GEMSens MCF7. The levels of Numb, and Numb-L-[P]-Ser265 were similar in GEMRes and GEMSens MCF7 cells. Only the levels of Numb-L (long)-Ser295 decreased slightly. This finding suggests that Notch-1 cleavage to TMIC is inhibited in GEMRes MCF7 cells. PBMC activated by natural immunogenic peptides Notch-1 (2112-2120) and Numb-1 (87-95) eliminated NICDpositive, CD24hi CD24lo MCF7 cells. It is likely that the immunogenic Numb-1 peptide in MCF7 cells originated from Numb, [P]-lated by an unknown kinase, because staurosporine but not wortmannin and MAPK-inhibitors decreased peptide presentation. Numb and Notch are antagonistic proteins which degrade each other to stop and activate cell proliferation, resp. Their peptides are presented alternatively. Targeting both antagonistic proteins should be useful to prevent metastases in patients whose tumors are resistant to conventional treatments.

OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)
 REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2009:336394 CAPLUS
 DOCUMENT NUMBER: 150:327907
 TITLE: Determining disease location, identifying immune system failure, and/or detg. treatments based on disease location or immune system failure
 INVENTOR(S): Zeskind, Benjamin J.
 PATENT ASSIGNEE(S): Immuneering Corporation, USA
 SOURCE: PCT Int. Appl., 39pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 2009035631</u>	A1	20090319	<u>WO 2008-US10611</u>	20080911
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
<u>US 20100310511</u>	A1	20101209	<u>US 2010-718905</u>	20100305
PRIORITY APPLN. INFO.:			<u>US 2007-993270P</u>	P 20070911
			<u>WO 2008-US10611</u>	A1 20080911

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The disclosed invention relates to methods and app. for diagnosing and treating human disease, including infection, allergy, and injury. Methods

comprise analyzing ≥ 1 elements, markers, ligands, or other characteristics of the immune system of a body (e.g., of a human or other animal), and based on the anal., detg. a location of disease, identifying immune system failure, and/or detg. treatments based on disease location or immune system failure. All or a part of the immune system process may be analyzed to identify specific features of the immune system, e.g., which may indicate that the disease will evade the immune system and produce a neg. outcome. Therapy may be employed to correct immune system failure rather than addressing the disease directly. The following illustrative embodiment shows steps in a method for analyzing immune system characteristics and detg. an immune state: (1) does acute phase activation occur (2) are natural killer cells activated (3) are macrophages activated and presenting the disease antigen (4) are dendritic cells activated and presenting the disease antigen (5) are dendritic cells conveying disease location via sol. factors (6) are T cells activated against the antigen (7) are T cells expressing the appropriate selectin ligands or cytokine receptors for tissue-specific homing (8) are T cells expressing the appropriate integrins for tissue-specific homing and (9) are the appropriate gradients present to enable T cells to home to the disease site.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 5 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2007:1167563 CAPLUS
 DOCUMENT NUMBER: 149:198054
 TITLE: Variation in the ligand binding domains of the CD94/**NKG2** family of receptors in the squirrel monkey
 AUTHOR(S): LaBonte, Michelle L.; Russo, Joanne; Freitas, Stephanie; Keighley, Dawn
 CORPORATE SOURCE: Department of Biological Sciences, Bridgewater State College, Bridgewater, MA, 02325, USA
 SOURCE: Immunogenetics (2007), 59(10), 799-811
 CODEN: IMNGBK; ISSN: 0093-7711
 PUBLISHER: Springer
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Natural killer cells are regulated, in part, by cell surface expression of the inhibitory CD94/NKG2A heterodimer and the activating CD94/NKG2C heterodimer. In the present study, we characterize the CD94/**NKG2** family in the squirrel monkey, a New World monkey species. Full-length CD94, NKG2A, and NKG2CE complementary DNA mols. were identified in three unrelated squirrel monkeys. Three alternatively spliced forms of CD94 were detected in which part of intron 4 was included in the mature transcript, suggesting evolutionary pressure for changes in the corresponding loop 3 region of the lectin domain in squirrel monkeys. Squirrel monkey NKG2A contains a three-nucleotide indel that results in an addnl. amino acid in the predicted NKG2A protein compared to NKG2A in other species. This NKG2A insertion tracks to loop five of the lectin domain, as is seen with the recently described marmoset NKG2CE indel. Transmembrane-deleted forms of CD94 and NKG2CE were also expressed in the squirrel monkey. Anal. of full-length squirrel monkey and addnl. primate CD94/**NKG2** sequences demonstrated statistically significant increases in the Ka/Ks ratio in the putative major histocompatibility complex E (MHC-E) binding domain compared to the non-binding domain. Furthermore, pos. selection was detected in the MHC-E binding domain of primate **NKG2** family members, and purifying selection was detected in the primate CD94 binding domain. Purifying selection was also detected in the nonbinding

domains of primate CD94 and **NKG2** mols.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2007:263823 CAPLUS
DOCUMENT NUMBER: 147:500645
TITLE: Complexity in the cattle CD94/**NKG2** gene families
AUTHOR(S): Birch, James; Ellis, Shirley A.
CORPORATE SOURCE: Immunology Division, Institute for Animal Health, Compton, RG20 7NN, UK
SOURCE: Immunogenetics (2007), 59(4), 273-280
CODEN: IMNGBK; ISSN: 0093-7711
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Natural killer cell responses are controlled to a large extent by the interaction of an array of inhibitory and activating receptors with their ligands. The mostly nonpolymorphic CD94/**NKG2** receptors in both humans and mice were shown to recognize a single nonclassical MHC class I mol. in each case. Here, the authors describe the CD94/**NKG2** gene family in cattle. **NKG2** and CD94 sequences were amplified from cDNA derived from 4 animals. Four CD94 sequences, 10 NKG2A, and 3 NKG2C sequences were identified in total. In contrast to human, the authors show that cattle have multiple distinct NKG2A genes, some of which show minor allelic variation. All of the sequences designated NKG2A have 2 tyrosine-based inhibitory motifs in the cytoplasmic domain and one putative gene has, in addn., a charged residue in the transmembrane domain. NKG2C appears to be essentially monomorphic in cattle. All of the NKG2A sequences are similar apart from NKG2A-01, which, in contrast, shares the majority of its carbohydrate recognition domain with **NKG2**-C. Most of the genes appear to generate multiple alternatively spliced forms. Thus, the CD94/NKG2A heterodimers in cattle, in contrast to other species, are binding several different ligands. Because NKG2C is not polymorphic, this raises questions as to the combined functional capacity of the CD94/**NKG2** gene families in cattle.

OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2005:1297676 CAPLUS
DOCUMENT NUMBER: 144:366899
TITLE: Microarray and real-time RT-PCR analyses of a novel set of differentially expressed human genes in ECV304 endothelial-like cells infected with dengue virus type 2
AUTHOR(S): Liew, Kingsley J. L.; Chow, Vincent T. K.
CORPORATE SOURCE: Human Genome Laboratory, Department of Microbiology, Yong Loo Lin School of Medicine, National University of Singapore, Kent Ridge, 117597, Singapore
SOURCE: Journal of Virological Methods (2006), 131(1), 47-57
CODEN: JVMEHD; ISSN: 0166-0934
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal

LANGUAGE: English

AB The cellular and mol. pathways of dengue infection have not been as intensively studied compared to the host immunol. responses. Changes in mRNA expression levels of ECV304 human endothelial-like cells following infection with the virulent New Guinea C strain of dengue virus type 2 were analyzed by a microarray system comprising 7600 oligonucleotide cDNAs. After normalization against the uninfected control using two independent software programs, 111 genes exhibited at least a 1.5-fold difference in expression level. Out of these, 21 mRNAs were upregulated while 90 mRNAs were downregulated. Quant. real-time RT-PCR was then performed to det. the expression patterns of 15 selected genes of interest involved in the cell cycle (MAD3), apoptosis (RIPK3, PDCD8), cellular receptors (H963, CCR7, KLRC3), transcriptional regulation (RUNX3, HNF4G, MIZ1), signal transduction (HSP27, TRIP, MAP4K4), enzymes (angiotensinogen), protein transport (AP4M1), and cytoskeleton (ACTA2). Dengue virus infection resulted in the downregulation of the C-terminal alternatively spliced p53 variant, the pro-apoptotic IG20 and IG20-SV2 isoforms, and the Fas apoptosis inhibitory mol. (FAIM). Most of the real-time RT-PCR data showed concordance with the normalized microarray data. Hence, real-time RT-PCR validation of high-throughput gene microarray screening is important and necessary before further conclusions on gene expression can be drawn. This study elucidated novel information on the complex responses at the transcriptional level in susceptible human endothelial-like cells induced by a virulent dengue virus strain implicated in the pathogenesis of dengue and/or its complications.

OS.CITING REF COUNT: 19 THERE ARE 19 CAPLUS RECORDS THAT CITE THIS RECORD (19 CITINGS)

REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2005:581031 CAPLUS

DOCUMENT NUMBER: 143:131542

TITLE: IFN- γ -mediated negative feedback regulation of NKT-cell function by CD94/**NKG2**

AUTHOR(S): Ota, Tsuyoshi; Takeda, Kazuyoshi; Akiba, Hisaya; Hayakawa, Yoshihiro; Ogasawara, Kouetsu; Ikarashi, Yoshinori; Miyake, Sachiko; Wakasugi, Hiro; Yamamura, Takashi; Kronenberg, Mitchell; Raulet, David H.; Kinoshita, Katsuyuki; Yagita, Hideo; Smyth, Mark J.; Okumura, Ko

CORPORATE SOURCE: Departments of Immunology, and Obstetrics and Gynecology, Juntendo University School of Medicine, Tokyo, Japan

SOURCE: Blood (2005), 106(1), 184-192
CODEN: BLOOAW; ISSN: 0006-4971

PUBLISHER: American Society of Hematology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Activation of invariant natural killer T (iNKT) cells with CD1d-restricted T-cell receptor (TCR) ligands is a powerful means to modulate various immune responses. However, the iNKT-cell response is of limited duration and iNKT cells appear refractory to secondary stimulation. Here we show that the CD94/NKG2A inhibitory receptor plays a crit. role in down-regulating iNKT-cell responses. Both TCR and NK-cell receptors expressed by iNKT cells were rapidly down-modulated by priming with α -galactosyl-ceramide (α -GalCer) or its analog OCH [(2S,3S,4R)-1-O-(α -D-galactopyranosyl)-N-tetracosanoyl-2-amino-

1,3,4-nonanetriol]. TCR and CD28 were re-expressed more rapidly than the inhibitory NK-cell receptors CD94/NKG2A and Ly49, temporally rendering the primed iNKT cells hyperreactive to ligand restimulation. Of interest, α -GalCer was inferior to OCH in priming iNKT cells for subsequent restimulation because α -GalCer-induced interferon γ (IFN- γ) up-regulated Qa-1b expression and Qa-1b in turn inhibited iNKT-cell activity via its interaction with the inhibitory CD94/NKG2A receptor. Blockade of the CD94/NKG2-Qa-1b interaction markedly augmented recall and primary responses of iNKT cells. This is the first report to show the crit. role for NK-cell receptors in controlling iNKT-cell responses and provides a novel strategy to augment the therapeutic effect of iNKT cells by priming with OCH or blocking of the CD94/NKG2A inhibitory pathway in clin. applications.

OS.CITING REF COUNT: 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS RECORD (20 CITINGS)
 REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2005:153931 CAPLUS
 DOCUMENT NUMBER: 142:353794
 TITLE: Interactions between NKG2x Immunoreceptors and HLA-E Ligands Display Overlapping Affinities and Thermodynamics
 AUTHOR(S): Kaiser, Brett K.; Barahmand-pour, Fariba; Paulsene, Wendy; Medley, Scott; Geraghty, Daniel E.; Strong, Roland K.
 CORPORATE SOURCE: Divisions of Basic Sciences and Clinical Research, Fred Hutchinson Cancer Research Center, Seattle, WA, 98109, USA
 SOURCE: Journal of Immunology (2005), 174(5), 2878-2884
 CODEN: JOIMA3; ISSN: 0022-1767
 PUBLISHER: American Association of Immunologists
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The NKG2x/CD94 family of C-type lectin-like immunoreceptors (x = A, B, C, E, and H) mediates surveillance of MHC class Ia cell surface expression, often dysregulated during infection or tumorigenesis, by recognizing the MHC class Ib protein HLA-E that specifically presents peptides derived from class Ia leader sequences. Here, the authors det. the affinities and interaction thermodyn. between 3 NKG2x/CD94 receptors (NKG2A, NKG2C, and NKG2E) and complexes of HLA-E with 4 representative peptides. Inhibitory NKG2A/CD94 and activating NKG2E/CD94 receptors bind HLA-E with indistinguishable affinities, but with significantly higher affinities than the activating NKG2C/CD94 receptor. Despite minor sequence differences, the peptide presented by HLA-E significantly influenced the affinities; HLA-E allelic differences had no effect. These results reveal important constraints on the integration of opposing activating and inhibitory signals driving NK cell effector functions.

OS.CITING REF COUNT: 40 THERE ARE 40 CAPLUS RECORDS THAT CITE THIS RECORD (40 CITINGS)
 REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2005:112755 CAPLUS

DOCUMENT NUMBER: 142:153476
 TITLE: Gene expression profiles and biomarkers for the detection of depression-related and other disease-related gene transcripts in blood
 INVENTOR(S): Liew, Choong-chin
 PATENT ASSIGNEE(S): Chondrogene Limited, Can.
 SOURCE: U.S. Pat. Appl. Publ., 154 pp., Cont.-in-part of U.S. Ser. No. 802,875.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 51
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>US 20040265868</u>	A1	20041230	<u>US 2004-812702</u>	20040330
<u>CA 2702148</u>	A1	20000713	<u>CA 2000-2702148</u>	20000105
<u>US 20040014059</u>	A1	20040122	<u>US 2002-268730</u>	20021009
<u>US 7598031</u>	B2	20091006		
<u>US 20070031841</u>	A1	20070208	<u>US 2003-601518</u>	20030620
<u>US 20060134635</u>	A1	20060622	<u>US 2004-802875</u>	20040312
<u>US 20050191637</u>	A1	20050901	<u>US 2004-803737</u>	20040318
<u>US 20050196762</u>	A1	20050908	<u>US 2004-803759</u>	20040318
<u>US 20050196763</u>	A1	20050908	<u>US 2004-803857</u>	20040318
<u>US 20050196764</u>	A1	20050908	<u>US 2004-803858</u>	20040318
<u>US 7662558</u>	B2	20100216		
<u>US 20050208505</u>	A1	20050922	<u>US 2004-803648</u>	20040318
<u>US 20040265868</u>	A1	20041230	<u>US 2004-812702</u>	20040330
<u>US 20100092983</u>	A1	20100415	<u>US 2009-573863</u>	20091005
<u>US 20100092984</u>	A1	20100415	<u>US 2009-573865</u>	20091005
<u>US 20100124745</u>	A1	20100520	<u>US 2009-573856</u>	20091005
<u>US 20100124746</u>	A1	20100520	<u>US 2009-587382</u>	20091005
<u>US 20100203520</u>	A1	20100812	<u>US 2009-587385</u>	20091005
<u>US 20100203519</u>	A1	20100812	<u>US 2009-587384</u>	20091006
<u>US 20110003294</u>	A1	20110106	<u>US 2010-757918</u>	20100409
<u>US 20110003295</u>	A1	20110106	<u>US 2010-757921</u>	20100409
<u>US 20110003296</u>	A1	20110106	<u>US 2010-757928</u>	20100409
<u>US 20110003297</u>	A1	20110106	<u>US 2010-757930</u>	20100409
<u>US 20110003298</u>	A1	20110106	<u>US 2010-757931</u>	20100409
<u>US 20110008779</u>	A1	20110113	<u>US 2010-757914</u>	20100409
<u>US 20110008780</u>	A1	20110113	<u>US 2010-757925</u>	20100409
<u>US 20110014614</u>	A1	20110120	<u>US 2010-757934</u>	20100409
<u>US 20110059447</u>	A1	20110310	<u>US 2010-757923</u>	20100409
<u>PRIORITY APPLN. INFO.:</u>			<u>US 2004-802875</u>	A2 20040312
			<u>US 2003-601518</u>	A2 20030620
			<u>US 2002-268730</u>	A2 20021009
			<u>US 2000-477148</u>	B1 20000104
			<u>US 1999-115125P</u>	P 19990106
			<u>US 2004-812702</u>	20040330
			<u>CA 2000-2359816</u>	A3 20000105
			<u>US 2001-271955P</u>	P 20010228
			<u>US 2001-275017P</u>	P 20010312
			<u>US 2001-305340P</u>	P 20010713
			<u>US 2002-85783</u>	A2 20020228
			<u>US 2009-573856</u>	A1 20091005
			<u>US 2009-573863</u>	A1 20091005
			<u>US 2009-587382</u>	A1 20091005
			<u>US 2009-587385</u>	A1 20091005
			<u>US 2009-587384</u>	A1 20091006

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention is directed to detection and measurement of gene transcripts and their equiv. nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing, and monitoring diseases, and in particular mental depression, using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially expressed gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstr. record is one of 3 records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.].

L16 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2005:112752 CAPLUS
 DOCUMENT NUMBER: 142:153475
 TITLE: Gene expression profiles and biomarkers for the detection of depression-related and other disease-related gene transcripts in blood
 INVENTOR(S): Liew, Choong-Chin
 PATENT ASSIGNEE(S): Chondrogene Limited, Can.
 SOURCE: U.S. Pat. Appl. Publ., 154 pp., Cont.-in-part of U.S. Ser. No. 802,875.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 51
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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<u>US 20040265868</u>	A1	20041230	<u>US 2004-812702</u>	20040330
<u>CA 2702148</u>	A1	20000713	<u>CA 2000-2702148</u>	20000105
<u>US 20040014059</u>	A1	20040122	<u>US 2002-268730</u>	20021009
<u>US 7598031</u>	B2	20091006		
<u>US 20070031841</u>	A1	20070208	<u>US 2003-601518</u>	20030620
<u>US 20060134635</u>	A1	20060622	<u>US 2004-802875</u>	20040312
<u>US 20050191637</u>	A1	20050901	<u>US 2004-803737</u>	20040318
<u>US 20050196762</u>	A1	20050908	<u>US 2004-803759</u>	20040318
<u>US 20050196763</u>	A1	20050908	<u>US 2004-803857</u>	20040318
<u>US 20050196764</u>	A1	20050908	<u>US 2004-803858</u>	20040318
<u>US 7662558</u>	B2	20100216		
<u>US 20050208505</u>	A1	20050922	<u>US 2004-803648</u>	20040318
<u>US 20040265868</u>	A1	20041230	<u>US 2004-812702</u>	20040330
<u>US 20100092983</u>	A1	20100415	<u>US 2009-573863</u>	20091005
<u>US 20100092984</u>	A1	20100415	<u>US 2009-573865</u>	20091005
<u>US 20100124745</u>	A1	20100520	<u>US 2009-573856</u>	20091005
<u>US 20100124746</u>	A1	20100520	<u>US 2009-587382</u>	20091005
<u>US 20100203520</u>	A1	20100812	<u>US 2009-587385</u>	20091005
<u>US 20100203519</u>	A1	20100812	<u>US 2009-587384</u>	20091006
<u>US 20110003294</u>	A1	20110106	<u>US 2010-757918</u>	20100409
<u>US 20110003295</u>	A1	20110106	<u>US 2010-757921</u>	20100409

<u>US 20110003296</u>	A1	20110106	<u>US 2010-757928</u>	20100409
<u>US 20110003297</u>	A1	20110106	<u>US 2010-757930</u>	20100409
<u>US 20110003298</u>	A1	20110106	<u>US 2010-757931</u>	20100409
<u>US 20110008779</u>	A1	20110113	<u>US 2010-757914</u>	20100409
<u>US 20110008780</u>	A1	20110113	<u>US 2010-757925</u>	20100409
<u>US 20110014614</u>	A1	20110120	<u>US 2010-757934</u>	20100409
<u>US 20110059447</u>	A1	20110310	<u>US 2010-757923</u>	20100409
<u>PRIORITY APPLN. INFO.:</u>			<u>US 2004-802875</u>	A2 20040312
			<u>US 2003-601518</u>	A2 20030620
			<u>US 2002-268730</u>	A2 20021009
			<u>US 2000-477148</u>	B1 20000104
			<u>US 1999-115125P</u>	P 19990106
			<u>US 2004-812702</u>	20040330
			<u>CA 2000-2359816</u>	A3 20000105
			<u>US 2001-271955P</u>	P 20010228
			<u>US 2001-275017P</u>	P 20010312
			<u>US 2001-305340P</u>	P 20010713
			<u>US 2002-85783</u>	A2 20020228
			<u>US 2009-573856</u>	A1 20091005
			<u>US 2009-573863</u>	A1 20091005
			<u>US 2009-587382</u>	A1 20091005
			<u>US 2009-587385</u>	A1 20091005
			<u>US 2009-587384</u>	A1 20091006

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention is directed to detection and measurement of gene transcripts and their equiv. nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing, and monitoring diseases, and in particular mental depression, using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially expressed gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstr. record is one of 3 records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.].

OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD
(5 CITINGS)

L16 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2005:1997 CAPLUS
DOCUMENT NUMBER: 142:111841
TITLE: Gene expression profiles and biomarkers for the detection of depression-related and other disease-related gene transcripts in blood
INVENTOR(S): Liew, Choong-Chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 154 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 51

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040265868	A1	20041230	US 2004-812702	20040330
CA 2702148	A1	20000713	CA 2000-2702148	20000105
US 20040014059	A1	20040122	US 2002-268730	20021009
US 7598031	B2	20091006		
US 20070031841	A1	20070208	US 2003-601518	20030620
US 20060134635	A1	20060622	US 2004-802875	20040312
US 20050191637	A1	20050901	US 2004-803737	20040318
US 20050196762	A1	20050908	US 2004-803759	20040318
US 20050196763	A1	20050908	US 2004-803857	20040318
US 20050196764	A1	20050908	US 2004-803858	20040318
US 7662558	B2	20100216		
US 20050208505	A1	20050922	US 2004-803648	20040318
US 20040265868	A1	20041230	US 2004-812702	20040330
US 20040265868	A1	20041230	US 2004-812702	20040330
US 20100092983	A1	20100415	US 2009-573863	20091005
US 20100092984	A1	20100415	US 2009-573865	20091005
US 20100124745	A1	20100520	US 2009-573856	20091005
US 20100124746	A1	20100520	US 2009-587382	20091005
US 20100203520	A1	20100812	US 2009-587385	20091005
US 20100203519	A1	20100812	US 2009-587384	20091006
US 20110003294	A1	20110106	US 2010-757918	20100409
US 20110003295	A1	20110106	US 2010-757921	20100409
US 20110003296	A1	20110106	US 2010-757928	20100409
US 20110003297	A1	20110106	US 2010-757930	20100409
US 20110003298	A1	20110106	US 2010-757931	20100409
US 20110008779	A1	20110113	US 2010-757914	20100409
US 20110008780	A1	20110113	US 2010-757925	20100409
US 20110014614	A1	20110120	US 2010-757934	20100409
US 20110059447	A1	20110310	US 2010-757923	20100409
<u>PRIORITY APPLN. INFO.:</u>			US 1999-115125P	P 19990106
			US 2000-477148	B1 20000104
			US 2002-268730	A2 20021009
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			US 2004-802875	A2 20040312
			CA 2000-2359816	A3 20000105
			US 2001-271955P	P 20010228
			US 2001-275017P	P 20010312
			US 2001-305340P	P 20010713
			US 2002-85783	A2 20020228
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			US 2009-573856	A1 20091005
			US 2009-573863	A1 20091005
			US 2009-587382	A1 20091005
			US 2009-587385	A1 20091005
			US 2009-587384	A1 20091006

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention is directed to detection and measurement of gene transcripts and their equiv. nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing, and monitoring diseases, and in particular mental depression, using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially expressed gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression

syndrome. The present invention describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstr. record is one of 3 records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.].

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L16 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2004:1045842 CAPLUS
 DOCUMENT NUMBER: 142:333926
 TITLE: Analysis of gene expression profiles of hepatocellular carcinomas with regard to 18F-fluorodeoxyglucose uptake pattern on positron emission tomography
 AUTHOR(S): Lee, Jong Doo; Yun, Mijin; Lee, Jae Myun; Choi, Youjeong; Choi, Youn-Hee; Kim, Ji Su; Kim, Se Jong; Kim, Kyung Sik; Yang, Woo Ick; Park, Young Nyun; Han, Kwang-Hyub; Lee, Woo Jung; Yoo, Naechun; Lim, Sang Moo; Park, Jeon Han
 CORPORATE SOURCE: Division of Nuclear Medicine, Department of Diagnostic Radiology, Yonsei University College of Medicine, Seoul, S. Korea
 SOURCE: European Journal of Nuclear Medicine and Molecular Imaging (2004), 31(12), 1621-1630
 CODEN: EJNMA6; ISSN: 1619-7070
 PUBLISHER: Springer GmbH
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Purpose: 18F-fluorodeoxyglucose (FDG) uptake on positron emission tomog. (PET) scan has been found to reflect tumor aggressiveness and prognosis in various types of cancer. In this study, the gene expression profiles of hepatocellular carcinomas (HCCs) were evaluated to det. whether HCCs with high 18F-FDG uptake have more aggressive biol. potential than those with low uptake. Methods: Surgical specimens were obtained from ten patients with HCC (six males and four females, age range 38-68 years). The tumor samples were divided into two groups based on the 18F-FDG PET scan findings: high 18F-FDG uptake (n=4) and low 18F-FDG uptake (n=6). Results: The pathol. tumor grade was closely correlated with the 18F-FDG uptake pattern: HCCs with high 18F-FDG uptake were pathol. Edmondson-Steiner grade III, while those with low uptake were either grade II or grade II with a focal area of grade III. The total RNA was extd. from the frozen tissues of all HCCs (n=10) and adjacent non-cancerous tissue (n=7). The gene expression profiles were evaluated using an oligoDNA microarray. The HCCs with high 18F-FDG uptake showed increased expression of 11 genes-including vascular cell adhesion mol.-1, vinexin beta and core 1 UDP-galactose:N-acetylgalactosamine-alpha-R-beta 1,3-galactosyltransferase and the natural killer cell inhibitory receptor-compared to those with low uptake (p<0.005). Nine genes, including regulator of mitotic spindle assembly 1, grb2-related adaptor protein and β -1,3-N-acetylglucosaminyltransferase, were repressed. Conclusion: Gene expression is closely related to cell survival, cell-to-cell adhesion or cell spreading; therefore, HCCs with high 18F-FDG uptake appear to have more aggressive biol. properties than those with low uptake.

OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2003:288979 CAPLUS
 DOCUMENT NUMBER: 138:336280
 TITLE: Variations of human killer cell lectin-like receptors: common occurrence of **NKG2**-C deletion in the general population
 AUTHOR(S): Hikami, K.; Tsuchiya, N.; Yabe, T.; Tokunaga, K.
 CORPORATE SOURCE: Department of Human Genetics, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan
 SOURCE: Genes and Immunity (2003), 4(2), 160-167
 CODEN: GEIMA2; ISSN: 1466-4879
 PUBLISHER: Nature Publishing Group
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB CD94 and **NKG2** are members of the NK cell receptor families, and are encoded in the natural killer gene complex (NKC) on human chromosome 12p12-13, one of the candidate chromosomal regions for rheumatic diseases. To examine a possible assocn. between variations in CD94 and **NKG2** genes and genetic susceptibility to rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), the authors carried out a systematic polymorphism screening of **NKG2**-A (KLRC1), **NKG2**-C (KLRC2) and CD94 (KLRD1) genes on a population basis. In **NKG2**-A, previously considered to be highly conserved, 10 polymorphisms in the non-coding region and introns, as well as one rare variation leading to an amino acid substitution within the transmembrane region, c.238T>A (Cys80Ser), were detected. In **NKG2**-C, in addn. to the previously described two nonsynonymous substitutions, c.5G>A (Ser2Asn) and c.305C>T (Ser102Phe), two polymorphisms were newly detected in the non-coding region. In CD94, only one single nucleotide substitution was identified in the 5' untranslated region. When the patients and healthy individuals were genotyped for these variations, no significant assocn. was obsd. However, although statistically not significant, **NKG2**-A c.238T>A (Cys80Ser) was obsd. in three patients with RA, but in none of the healthy individuals and the patients with SLE. Unexpectedly, in the process of polymorphism screening, the authors identified homozygous deletion of **NKG2**-C in approx. 4.3% of healthy donors; under the assumption of Hardy-Weinberg equil., the allele frequency of **NKG2**-C deletion was estd. to be 20.7%. These results demonstrated that, although human **NKG2**-A, -C and CD94 are generally conserved with respect to amino acid sequences, **NKG2**-A is polymorphic in the non-coding region, and that the no. of genes encoded in the human NKC is variable among individuals, as previously shown for the leukocyte receptor complex (LRC), HLA and Fcγ receptor (FCGR) regions.

OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2003:129157 CAPLUS
 DOCUMENT NUMBER: 138:152237
 TITLE: Preferential Survival of CD8 T and NK Cells Expressing High Levels of CD94
 AUTHOR(S): Gunturi, Anasuya; Berg, Rance E.; Forman, James

CORPORATE SOURCE: Center for Immunology, University of Texas
Southwestern Medical Center, Dallas, TX, 75390, USA
SOURCE: Journal of Immunology (2003), 170(4), 1737-1745
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The Qa-1b/Qdm tetramer binds to CD94/**NKG2** receptors expressed at high levels on 50% of murine NK cells. Although very few CD8 T cells from naive mice express CD94/**NKG2** receptors, 50% of CD8 T cells taken from mice undergoing a secondary response against *Listeria monocytogenes* (LM) are CD94^{high} and bind the tetramer. Although CD94^{int} NK cells do not bind the tetramer, CD94^{int} CD8 T cells do, and this binding is dependent on the CD8 coreceptor. We found that the extent of apoptosis in CD8 T and NK cells was inversely related to the expression of CD94, with lower levels of apoptosis seen in CD94^{high} cells after 1-3 days of culture. The difference in CD8 T cell survival was evident as early as 6 h after culture and persisted until nearly all the CD94^{neg/int} cells were apoptotic by 48 h. In contrast, expression of inhibitory Ly-49A,G2,C/I mols. was assocd. with higher levels of apoptosis. Crosslinking CD94/**NKG2** receptors on CD8 T cells from a mouse undergoing an LM infection further reduced the percentage of apoptotic cells on the CD94-expressing populations, while crosslinking Ly-49I had no effect on CD8 T cells expressing Ly-49I. Crosslinking CD3 on CD8 T cells from a mouse undergoing a secondary LM infection increases the extent of apoptosis, but this is prevented by crosslinking CD94/**NKG2** receptors at the same time. Similar results were obsd. with NK cells in that the CD94^{high} population displayed less apoptosis than CD94^{int} cells after 1-3 days in culture. Therefore, the expression of CD94/**NKG2** is correlated with a lower level of apoptosis and may play an important role in the maintenance of CD8 T and NK cells.

OS.CITING REF COUNT: 45 THERE ARE 45 CAPLUS RECORDS THAT CITE THIS RECORD (45 CITINGS)
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2002:262037 CAPLUS
DOCUMENT NUMBER: 136:368105
TITLE: Expression of inhibitory receptors Ly49E and CD94/**NKG2** on fetal thymic and adult epidermal TCR V γ 3 lymphocytes
AUTHOR(S): Van Beneden, Katrien; De Creus, An; Stevenaert, Frederik; Debacker, Veronique; Plum, Jean; Leclercq, Georges
CORPORATE SOURCE: Department of Clinical Chemistry, Microbiology, University Hospital, University of Ghent, Ghent, B-9000, Belg.
SOURCE: Journal of Immunology (2002), 168(7), 3295-3302
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ly49 and CD94/**NKG2** inhibitory receptors are predominantly expressed on murine NK cells, but they are also expressed on a subpopulation of peripheral CD8 memory TCR $\alpha\beta$ lymphocytes. In this study the authors demonstrate that Ly49E and CD94/**NKG2** receptors are expressed on mature TCR V γ 3⁺ cells in the fetal thymus. Expression correlated

with a memory phenotype, such as expression of CD44, 2B4, and IL-2R β (CD122), and absence of IL-2R α (CD25) expression. No expression of Ly49A, C, D, G2, or I receptors was obsd. This phenotype is similar to that of fetal thymic NK cells. Skin-located V γ 3 T cells, the progeny of fetal thymic V γ 3 cells, also expressed CD94/**NKG2** and Ly49E but not the other members of the Ly49 family. The development and survival of Ly49E+ or CD94/**NKG2**+ V γ 3 T lymphocytes was not dependent upon expression of MHC class I mols. The cytotoxicity of TCR V γ 3 cells was inhibited when Qdm, the ligand for CD94/**NKG2**, was presented by Qalb-transfected target cells. Also, upon crosslinking of CD94/**NKG2** with mAb 3S9, TCR V γ 3 thymocytes were prevented from killing Fc γ R+ P815 target cells. These effects were most pronounced in the CD94/**NKG2**high subpopulation as compared with the CD94/**NKG2**low subpopulation of V γ 3 cells. Our data demonstrate that V γ 3 T cells expressing inhibitory Ly49E and CD94/**NKG2** receptors are mature and display a memory phenotype, and that CD94/**NKG2** functions as an inhibitory receptor on these T lymphocytes.

OS.CITING REF COUNT: 21 THERE ARE 21 CAPLUS RECORDS THAT CITE THIS RECORD (21 CITINGS)
 REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2001:738922 CAPLUS
 DOCUMENT NUMBER: 135:240444
 TITLE: Analysis of ligand for NK cell inhibitory receptors
 AUTHOR(S): Naoki, Matsumoto
 CORPORATE SOURCE: Grad. Sch. Frontier Sci., The Univ. Tokyo, Japan
 SOURCE: Ensho to Men'eki (2001), 9(5), 513-523
 CODEN: ENMEFA; ISSN: 0918-8371
 PUBLISHER: Sentan Igakusha
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: Japanese

AB A review with 29 refs., on the structure and functions of MHC class I receptors of NK cell, discussing; (1) MHC class I recognition by C-type lectin-like NK cell receptor Ly-49, (2) identification of the functional binding site for Ly-49A on the MHC class I mols., (3) mechanism of the recognition of the polymorphism in MHC class I antigens by Ly-49A, (4) recognition of nonclassical MHC class I mols. by C-type lectin-like receptor CD94/**NKG2**, (5) classification and structure of killer cell Ig-like receptors (KIR), (6) mechanism of the recognition of MHC class I mols. by KIR, and (7) recognition of MHC class I mols. by LIR-1.

L16 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2001:730469 CAPLUS
 DOCUMENT NUMBER: 136:84625
 TITLE: Biological insights into TCR $\gamma\delta$ + and TCR $\alpha\beta$ + intraepithelial lymphocytes provided by serial analysis of gene expression (SAGE)
 AUTHOR(S): Shires, John; Theodoridis, Efsthathios; Hayday, Adrian C.
 CORPORATE SOURCE: Peter Gorer Department of Immunobiology Guy's, King's, Medical School King's College, University of London, London, SE1 9RT, UK
 SOURCE: Immunity (2001), 15(3), 419-434
 CODEN: IUNIEH; ISSN: 1074-7613

PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Intraepithelial lymphocytes (IELs) are abundant, evolutionarily conserved T cells, commonly enriched in T cell receptor (TCR) $\gamma\delta$ expression. However, their primary functional potential and constitutive activation state are incompletely understood. To address this, serial anal. of gene expression (SAGE) was applied to murine TCR $\gamma\delta$ + and TCR $\alpha\beta$ + intestinal IELs directly ex vivo, identifying 15,574 unique transcripts that collectively portray an "activated yet resting," Th1-skewed, cytolytic, and immunoregulatory phenotype applicable to multiple subsets of gut IELs. Expression of granzymes, Fas ligand, RANTES, prothymosin β 4, junB, RGS1, Btg1, and related mols. is high, whereas expression of conventional cytokines and high-affinity cytokine receptors is low. Differentially expressed genes readily identify heterogeneity among TCR $\alpha\beta$ + IELs, whereas differences between resident TCR $\gamma\delta$ + IELs and TCR $\alpha\beta$ + IELs are less obvious.

OS.CITING REF COUNT: 120 THERE ARE 120 CAPLUS RECORDS THAT CITE THIS RECORD (120 CITINGS)

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2001:474865 CAPLUS

DOCUMENT NUMBER: 136:162043

TITLE: Genomic diversity of natural killer cell receptor genes in three populations

AUTHOR(S): Toneva, M.; Lepage, V.; Lafay, G.; Dulphy, N.; Busson, M.; Lester, S.; Vu-Trien, A.; Michaylova, A.; Naumova, E.; McCluskey, J.; Charron, D.

CORPORATE SOURCE: Division of Clinical and Transplantation Immunology, Medical University, Sofia, Bulg.

SOURCE: Tissue Antigens (2001), 57(4), 358-362
CODEN: TSANA2; ISSN: 0001-2815

PUBLISHER: Munksgaard International Publishers Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The distribution of genes encoding 11 killer cell Ig-like receptors (KIR) and 2 CD94:**NKG2** receptors in 32 Caucasians, 67 Australian Aborigines, and 59 Vietnamese were reported. The inhibitory and the activating KIR genes were found at different frequency in the 3 populations. No correlation was found between the polymorphism of the KIR genes and the HLA specificities of the tested samples. The most significant KIR assocns. were 2DL2 with 2DS2, 2DL2 with 2DS3, and 3DL1 with 2DS4 in all 3 study groups. In Caucasians and Vietnamese 2DS2 was assocd. with 2DS3 and 2DS1 with 3DS1. KIR 2DL1 was strongly assocd. with three other KIRs (2DL3, 3DL1 and 2DS4) in Aborigines. The distribution of the KIR phenotypes was different in the 3 populations. The AA1 phenotype was frequent in Vietnamese (42.4%) and Caucasians (31.2%), but very rare in Aborigines (1.5%). In contrast, the BB7 phenotype was very common for Aborigines (22.4%) and was absent in the 2 other groups. The data demonstrate that different assocns. and putative KIR haplotypes could be distinguished in different populations.

OS.CITING REF COUNT: 87 THERE ARE 87 CAPLUS RECORDS THAT CITE THIS RECORD (88 CITINGS)

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 2001:100077 CAPLUS
 DOCUMENT NUMBER: 134:264838
 TITLE: Functional analysis of the molecular factors
 controlling Qa1-mediated protection of target cells
 from NK lysis
 AUTHOR(S): Gays, Frances; Fraser, Karen P.; Toomey, Jennifer A.;
 Diamond, Austin G.; Millrain, Margaret M.; Dyson, P.
 Julian; Brooks, Colin G.
 CORPORATE SOURCE: Department of Microbiology and Immunology, The Medical
 School, Newcastle, NE2 4HH, UK
 SOURCE: Journal of Immunology (2001), 166(3), 1601-1610
 CODEN: JOIMA3; ISSN: 0022-1767
 PUBLISHER: American Association of Immunologists
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB CD94/**NKG2** receptors on mouse NK cells recognize the nonclassical class I
 mol. Qa1 and can deliver inhibitory signals that prevent NK cells from
 lysing Qa1-expressing cells. However, the exact circumstances under which
 Qa1 protects cells from NK lysis and, in particular, the role of the
 dominant Qa1-assocd. peptide, Qdm, are unclear. In this study, the
 authors examd. in detail the lysis of Qa1-expressing cells by fetal NK
 cells that express CD94/**NKG2** receptors for Qa1 but that lack receptors
 for classical class I mols. Whereas mouse L cells and human C1R cells
 transfected with Qa1 were resistant to lysis by these effectors,
 Qa1-transfected TAP-deficient human T2 cells showed no resistance despite
 expressing high levels of surface Qa1. However, these cells could be
 efficiently protected by exposure to low concns. of Qdm peptide or certain
 Qdm-related peptides. By contrast, even prolonged exposure of
 TAP-deficient RMA/S cells to high doses of Qdm peptide failed to induce
 levels of surface Qa1 detectable with a Qa1-specific mAb or to protect
 them from NK lysis, although such treatment induced sensitivity to lysis
 by Qa1-specific CTL. Collectively, these findings indicate that high
 surface expression of Qa1 is necessary but not sufficient for protection,
 and that effective protection requires the expression of sufficient levels
 of suitable Qa1-peptide complexes to overcome activatory signals. Results
 obtained with a series of substituted Qdm peptides suggest that residues
 at positions 3, 4, 5, and 8 of the Qdm sequence, AMAPRTLLL, are
 important for recognition of Qa1-Qdm complexes by inhibitory CD94/**NKG2**
 receptors.

OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS
 RECORD (15 CITINGS)
 REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 1999:452525 CAPLUS
 DOCUMENT NUMBER: 131:321144
 TITLE: Why so many coinhibitory receptors?
 AUTHOR(S): Sinclair, N. R. StC.
 CORPORATE SOURCE: Department of Microbiology and Immunology, The
 University of Western Ontario, London, ON, N6A 5C1,
 Can.
 SOURCE: Scandinavian Journal of Immunology (1999), 50(1),
 10-13

CODEN: SJIMAX; ISSN: 0300-9475
 PUBLISHER: Blackwell Science Ltd.
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

AB A review and discussion with 28 refs. Receptors that display neg. signaling functions on lymphocytes and other cells of the reticuloendothelial system now no. about 30. These neg. receptors are transmembrane glycoproteins activated by phosphorylation of a tyrosine residue in immunoreceptor tyrosine-based inhibitory motifs that bind various phosphatases to induce dominant neg. signals. Since these receptors are armed by the action of activating receptors and inhibit signaling by activating receptors, we have termed them coinhibitory receptors and the neg. outcome is coinhibition. Coinhibitory receptors and some inhibitory mediators include FcγRIIB, CTLA-4, CD5, CD22, p58/70/140 KIR, gp49B1/gp91, PIRB1-5, LAIR-1, NKB1, Ly49 A/C/E/F/G, **NKG2**-A/B APC-R, CD66, CD72, PD-1, SHPS-1, SIRP-α1, ILT1-5, MIR7,10, hMIR(HM18), hMIR(HM9), LIR1-3,5,8, Fas (CD95), TGFβ-R, TNF-R1, IFNγ-R (α and β chains), mast cell function Ag, H2-M, HLA-DM, CD1, CD1-d, CD46, c-cbl, Pyk2/FADK2, P130 Ca rel prot, PGDF-R, LIF, LIF-R, CIS, SOCS13 and 5, and others are being defined regularly. This long list suggests that coinhibitors are needed not only for self-nonsel discrimination, but also for control of ongoing responses to foreign antigens so that infectious agents are ideally dealt with by an appropriate level of immune responses to nonself and an appropriate amt. of immunopathol. and sickness behavior.

OS.CITING REF COUNT: 21 THERE ARE 21 CAPLUS RECORDS THAT CITE THIS RECORD (21 CITINGS)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 1998:685732 CAPLUS
 DOCUMENT NUMBER: 129:288814
 ORIGINAL REFERENCE NO.: 129:58829a,58832a
 TITLE: HLA-E is the ligand for the natural killer cell CD94/**NKG2** receptors
 AUTHOR(S): Posch, Phillip E.; Borrego, Francisco; Brooks, Andrew G.; Coligan, John E.
 CORPORATE SOURCE: Structural Biology Section, National Inst. Allergy Infectious Disease, National Inst. Health, Rockville, MD, 20852, USA
 SOURCE: Journal of Biomedical Science (Basel) (1998), 5(5), 321-331
 CODEN: JBCIEA; ISSN: 1021-7770
 PUBLISHER: S. Karger AG
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

AB A review is given with 102 refs. CD94/**NKG2** is a recently described receptor present on natural killer (NK) cells and certain T cells that is composed of the CD94 chain covalently assocd. with a member of the **NKG2** family of mols. Both chains are glycosylated members of the C-type lectin superfamily. The CD94/**NKG2** receptors are functionally heterogeneous depending on which **NKG2** family member is assocd. with CD94. It was thought that CD94/**NKG2** receptors recognized a broad array of HLA-A, -B, and -C (classical), as well as the nonclassical HLA-G, MHC class I mols. Recent data have suggested that this receptor is specific for HLA-E complexed with a peptide derived from the signal sequence (residues 3-11) of certain classical MHC class I mols. Position 2 (residue 4)

in the signal sequence derived peptides appears pivotal in detg. whether the HLA-E/peptide complex confers resistance to NK-mediated lysis. The potential roles that the CD94/**NKG2**-HLA-E receptor ligand interaction might play in infection and tumor development are discussed.

OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)

L16 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 1998:162486 CAPLUS
 DOCUMENT NUMBER: 128:281696
 ORIGINAL REFERENCE NO.: 128:55769a,55772a
 TITLE: Recognition of human histocompatibility leukocyte antigen (HLA)-E complexed with HLA class I signal sequence-derived peptides by CD94/**NKG2** confers protection from natural killer cell-mediated lysis
 AUTHOR(S): Borrego, Francisco; Ulbrecht, Matthias; Weiss, Elisabeth H.; Coligan, John E.; Brooks, Andrew G.
 CORPORATE SOURCE: Laboratory of Molecular Structure, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Rockville, MD, 20852, USA
 SOURCE: Journal of Experimental Medicine (1998), 187(5), 813-818
 CODEN: JEMEAV; ISSN: 0022-1007
 PUBLISHER: Rockefeller University Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Human histocompatibility leukocyte antigen (HLA)-E is a nonclassical HLA class I mol., the gene for which is transcribed in most tissues. It has recently been reported that this mol. binds peptides derived from the signal sequence of HLA class I proteins; however, no function for HLA-E has yet been described. The authors show that natural killer (NK) cells can recognize target cells expressing HLA-E mols. on the cell surface and this interaction results in inhibition of the lytic process. Furthermore, HLA-E recognition is mediated primarily through the CD94/**NKG2**-A heterodimer, as CD94-specific, but not killer cell inhibitory receptor (KIR)-specific mAbs block HLA-E-mediated protection of target cells. Cell surface HLA-E could be increased by incubation with synthetic peptides corresponding to residues 3-11 from the signal sequences of a no. of HLA class I mols.; however, only peptides which contained a Met at position 2 were capable of conferring resistance to NK-mediated lysis, whereas those having Thr at position 2 had no effect. Interestingly, HLA class I mols. previously correlated with CD94/**NKG2** recognition all have Met at residue 4 of the signal sequence (position 2 of the HLA-E binding peptide), whereas those which have been reported not to interact with CD94/**NKG2** have Thr at this position. These data thus show a function for HLA-E and suggest an alternative explanation for the apparent broad reactivity of CD94/**NKG2** with HLA class I mols.; that CD94/**NKG2** interacts with HLA-E complexed with signal sequence peptides derived from "protective" HLA class I alleles rather than directly interacting with classical HLA class I proteins.

OS.CITING REF COUNT: 341 THERE ARE 341 CAPLUS RECORDS THAT CITE THIS RECORD (344 CITINGS)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2011 ACS on STN



ACCESSION NUMBER: 1993:162459 CAPLUS
 DOCUMENT NUMBER: 118:162459
 ORIGINAL REFERENCE NO.: 118:27705a
 TITLE: **NKG2** proteins of natural killer cells, cDNA encoding them, and methods for treatment of cancer or virus infection
 INVENTOR(S): Houchins, Jeffrey P.; Yabe, Toshio; McSherry, Cynthia M.; Bach, Fritz H.; Hofer, Erhard
 PATENT ASSIGNEE(S): University of Minnesota, USA; Sandoz Ltd.
 SOURCE: PCT Int. Appl., 61 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 9217198</u>	A1	19921015	<u>WO 1992-US2469</u>	19920327
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
<u>EP 585257</u>	A1	19940309	<u>EP 1992-909331</u>	19920327
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
<u>JP 06506358</u>	T	19940721	<u>JP 1992-508930</u>	19920327
<u>US 6262244</u>	B1	20010717	<u>US 1995-543246</u>	19951013
<u>PRIORITY APPLN. INFO.:</u>			<u>US 1991-676663</u>	A2 19910328
			<u>WO 1992-US2469</u>	W 19920327
			<u>US 1993-122514</u>	B1 19930924

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The cDNAs for **4 NKG2** proteins of human natural killer cells are cloned and sequenced. Antibodies to these proteins; chimeric antibodies recognizing **NKG2** protein and a cancer- or virus-specific antigen; **NKG2**-cytotoxic protein fusion proteins; and the use of these antibodies or chimeric proteins for treatment of cancer or virus infection are claimed. The **4** cDNAs represent a new mammalian gene family. These proteins displayed significant sequence similarity only with type II transmembrane proteins with C-type animal lectin domains. The **NKG2-C** protein was manufd. with transgenic Sf9 cells and the extracellular domain of this protein manufd. as a fusion protein in Escherichia coli.

OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD
 (8 CITINGS)

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